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Greetings from IJCP

As we navigate the ever-evolving landscape of pharmaceutical sciences, it is with great pleasure that I extend my warmest greetings to you in this edition of the International Journal of Community Pharmacy. Our commitment to advancing knowledge in pharmacy resonates strongly, and the array of research articles within these pages exemplifies the dedication and innovation thriving in the global community of pharmaceutical researchers.

1. Bridging the Gaps: Patient-Centric Approaches

The cornerstone of community pharmacy lies in its direct impact on patient care. In this issue, we explore groundbreaking studies elucidating patient-centric approaches that bridge the gaps between healthcare providers and individuals. From medication adherence interventions to the integration of digital health tools, the articles featured underscore the pivotal role community pharmacists play in enhancing overall health outcomes.

2. Pharmacological Frontiers: Unveiling Novel Therapeutics

Our journal proudly showcases the forefront of pharmacological research, unveiling novel therapeutics that have the potential to redefine treatment paradigms. Whether it be the discovery of new drug entities, exploration of innovative delivery systems, or the optimization of existing medications, the articles within this section provide a panoramic view of the diverse and dynamic nature of pharmaceutical research.

3. Community Pharmacy Practice: Innovations and Challenges

The practice of community pharmacy is not static; it evolves with the needs of the community it serves. Delve into this issue to explore the latest innovations and challenges in community pharmacy practice. From the implementation of advanced pharmaceutical services to navigating regulatory landscapes, our authors shed light on the multifaceted dimensions that shape the day-to-day operations of community pharmacies worldwide.

4. Global Collaborations: Driving Impactful Research

Research knows no borders, and in this edition, we highlight the significance of global collaborations in driving impactful research. The collaborative efforts showcased in these pages underscore the power of diverse perspectives and cross-cultural exchanges, enriching the discourse surrounding community pharmacy on a global scale.

As the editor, I express my sincere gratitude to the dedicated authors, esteemed reviewers, and the tireless editorial team for their unwavering commitment to excellence. Together, we continue to weave the tapestry of knowledge that propels the field of community pharmacy forward.

I invite you to immerse yourself in the wealth of insights and discoveries presented in this issue. May it inspire new ideas, spark collaborations, and contribute to the collective pursuit of advancing pharmaceutical science for the betterment of communities worldwide.

Warm regards,

Dr. Hanumanthachar Joshi
Editor-in-Chief
International Journal of Community Pharmacy

Review Article

# REVIEW ON TELEPHARMACY SERVICES: AN ADVANTAGE FOR RURAL COMMUNITIES

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**ABSTRACT:**

Nowadays internet is used by everyone, it is common in any domain and any business. The use of the Internet in the field of pharmacy is rapidly growing. Dispensing of medicines through tele pharmacy is a great idea, this would be more beneficial for rural people and emergency purposes. The purpose of this review is to create health education regarding tele pharmacy and its importance. Tele pharmacy and telemedicine are growing popular because some people are unable to get the medication in rural areas. Tele pharmacy has become an area of research as it provides access to healthcare services to rural patients. Tele pharmacy also helpful for the maintenance of patient records, treatments, monitoring of adverse drug reactions and case reports. The main purpose of this tele pharmacy is to provide medication for the rural people and all the populations. This article includes all the information about tele pharmacy and its service types.

**Keywords**: Tele pharmacy, Rural area, telemedicine, telecommunication, health services.

**INTRODUCTION:**

Tele pharmacy is the delivery of pharmaceutical care through telecommunication to patients in locations where they cannot have direct contact with a pharmacist. In this there are so many services including therapeutic drug monitoring, patient counselling, prior authorization refill of prescription drugs, monitoring of drug usage with the help of telecommunication and video conferencing. It plays a major role in reducing adverse drug reactions, medication cost, and treatment risk. In tele pharmacy service pharmacists may not be physically present at the location of the patient, but provide the medication. Tele pharmacy service dispenses the medication to people who are in remote areas and un available to

access the hospitals. This has been adopted by many healthcare institutions as an alternative strategy for expanding pharmacy for all people and this is the best method to achieve the highest standard of quality for delivering pharmacy services to rural communities, providing health education to promote safety and proper use of pharmaceuticals. Tele pharmacy is a new opportunity for pharmacists to grow and attach to technology that benefit patients to expand their role and access more people than ever. Tele pharmacy was officially first done by United States in 2001, out of the United States North Dakota became the first state to evaluate or conduct a study having 81 pharmacies, carried out at North Dakota State University later tele pharmacy services became available in China, Canada, Italy, Germany, Scotland, France, Denmark, Spain, and Egypt, out of these United states, Australia has largest exposure in reducing shortage in health services.

**OBJECTIVES:**

* To make the best quality healthcare available to rural communities.
* Reducing the time and money wasted by suppliers and patients.
* Provide home care and case monitoring.
* Reduce the cost of medical care.
* survey and tracking of diseases.

**TYPES OF TELEPHARMACY:**

The four types of tele pharmacy are;

**In-patient / remote order- entry review:**

In this type, a pharmacist is at remote locations and performs remote-order services for an in- patient pharmacy at a hospital. Pharmacist at remote level reviews the medication orders before the hospital staff administers the drugs to the patient, it is beneficial to hospitals, clinics, and health systems as it enables real-time medication order

examination and monitoring. This service is provided 24/7 by pharmacists.

**Remote dispensing**:

It is also called a retail communication tele pharmacy or outpatient. A retail communication tele pharmacy is a licensed pharmacy, staffed by a certified pharmacy technician. The pharmacist supervises the technician, reviews prescriptions, and performs his or her duties from a remote location via video conferencing or telecommunication. Many rural areas that are far away are unable to access these services due to geographical location, this method is convenient and easy access to for patients.

**IV admixture:**

The Joint Commission on Accreditation of Health Care Organizations (JCAHO) defines IV admixture as the preparation of a product or medication to a 50 ml / greater bottle of IV fluid. Pharmacists review the IV admixture remotely and save the time needed to suit up and enter the clean room to review the solution. Implementing an image-based tele pharmacy workflow in a clean room allows you to document each step of the process and reduce mistakes. It also reduces the time and can also save money.

**Remote counselling:**

In this type pharmacist provides counselling to the patients through secure live and interactive video conferencing or via telecommunications, by this method the patient can feel better and provide an opportunity for special counselling (HIV, AIDS, and other STDs) and various clinical interactions with pharmacists.

**TYPES OF TELEPHARMACY SERVICES:**

**Traditional pharmacy**:

These types of pharmacies consisted of both prescription and non-prescription drugs including beauty and other health-related products. In this type prescription is prepared at the same location and pharmacists provide the drug information, and utilization to the patient.

**Remote consultation sites:**

These types of pharmacy services are beneficial to rural communities and in this type, there is no prescription drug inventory at the site, it doesn't require a registered pharmacist. Here the prescriptions are taken and sent to central pharmacies, the medicines are supplied from central pharmacies to rural communities, patient education is through the audio and video counselling.

**Hospital telepharmacy:**

In these prescriptions that are issued in rural hospitals are electronically sent to the urban medical centre pharmacy, then the urban hospital pharmacist has access to review the patient's electronic records and check the prescription proper dosing etc. Then the medication is sent via an automatic dispensing device (ADD). A nurse in a rural hospital with access to ADD reviews the medication and labels and hands over medicine to the patient, the pharmacist at an urban hospital monitors electronically the verification process to check the restocking of ADD through video conferencing.

**Automated dispensing machines:**

pharmacist at the centre location upon receiving the drug order electronically or by fax, then the licensed pharmacist confirms the patient profile, proper drug utilization review, and finally instructs the Automated dispensing machine to release the medication. These automated dispensing machines have limited drug inventory and these are mainly used for urgent or first doses to the patient.

**BENEFIT FOR RURAL COMMUNITY:**

Tele pharmacy services have played a beneficial role in rural communities because due to geographical areas and the places where pharmacist, pharmacy services are limited. It also saves time, cost for the patient, in this tele pharmacy medication error rates are equal to or lower than in traditional pharmacy settings and patients who are living in remote areas are satisfied with tele pharmacy services. It was reported that most rural area people travelled more than 40 to 50 miles to get their prescriptions. So, introducing this system makes patients easy and more satisfied.

**ADVANTAGES:**

1. Reduced operations.
2. Economic benefits.
3. Patient satisfaction.
4. Effective patient counselling.
5. Overcome distance barriers.

6. Enhanced clinical role for pharmacists.

**DISADVANTAGES:**

1. Practical challenges.
2. Pharmacy regulation laws.
3. Security.
4. Operational difficulties.
5. In the ability to use technology.

**WORKING OF TELEPHARMACY**:

Prescriptions arrive at rural centres.

The prescription is verified and arrives at rural centres.

Rural centres are connected with urban centres.

Central pharmacists review the prescription and

release appropriate items with label.

The barcode is scanned at rural centres to ensure that

it matches the drug label.

After verifying barcode medicine is supplied to the

patient along with the label.

The central pharmacist provides detailed drug

information through a videoconference or telecommunication.

**TELEPHARMACY DURING COVID**

COVID patients avoid hospital care due to stay-at-home orders or fear of the virus. So, the use of tele pharmacy has been promoted during the COVID-19 pandemic. Tele pharmacy services during the pandemic have lot of benefits for the healthcare system and improved public health. Access to these services increases social distance and reduces the effect of infectious exposure.

**TELEPHARMACY IN INDIA**

In India health care was developed properly and there is a shortage of doctors, equipment, and staff. In India, 68% of people live in rural areas and 92 % of people in secondary care and tertiary care facilities are situated in urban areas. So the doctors can provide the prescription and consultations through tele pharmacy and tele medicine.

***e-sanjeevani:***

e-sanjeevani is a national telemedicine service a great initiative for all the people in India by the Union Ministry of Health and Family Welfare, Government of India in November 2019. Through this scheme free telemedicine service is provided. It is an alternative to the conventional physical consultations via digital platform.

It has crossed 8 crore consultations were received and 1 crore consultations are done within 5 weeks for better health care. In this doctor gives the electronic prescription to the patients.

**Consultation process of Assisted telemedicine of e-sanjeevani:**

- ✓ Visit the nearest Health and well-being centre
- ✓ Meet CHO
- ✓ CHO will create a case in e-sanjeevani
- ✓ Consult doctor/specialist virtually
- ✓ Gets e-prescription

**CONCLUSION:**

To reduce patient's time, money tele pharmacy is a great method that to deliver healthcare facilities and medication to people who are unable to access healthcare services in rural areas. Tele pharmacy plays a major role in reducing adverse drug reactions, medication costs, and treatment risks. This article includes all the information regarding tele pharmacy, types of tele pharmacy, models in tele pharmacy, advantages, and disadvantages, working of tele pharmacy, tele pharmacy during COVID, and tele pharmacy condition in India.

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Review Article

# A COMPREHENSIVE REVIEW ON FORMULATION AND EVALUATION OF HERBAL ANTI-AGEING CREAM USING POMEGRANATE SEED OIL

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**ABSTRACT:**

Anti-ageing creams are formulated using various natural and synthetic ingredients to counter the changes in the skin's structure and function that occur with ageing. Pomegranate oil, a natural ingredient rich in antioxidants and anti-inflammatory properties, has been used for various medicinal and cosmetic purposes. This review article aims to explore the formulation and evaluation of anti-ageing cream using pomegranate oil. The article provides an overview of the anti-ageing properties of pomegranate oil and the different formulations used to develop pomegranate oil-based anti-ageing creams. The article also discusses the evaluation methods used to test the efficacy of pomegranate oil-based anti-ageing creams. Pomegranate seed oil is a natural ingredient that has been used for various medicinal and cosmetic purposes. In this review article, we explore the formulation and evaluation of anti-ageing cream using pomegranate oil. The article provides an overview of the anti-ageing properties of pomegranate seed oil and the different formulations used to develops pomegranate seed oil-based anti-ageing creams. The article also discusses the evaluation methods used to test the efficacy of pomegranate seed oil-based anti-ageing creams. The results of the studies suggest that pomegranate seed oil-based anti-ageing creams can be effective in reducing the signs of ageing.

**Keywords** - Ageing, pomegranate seed oil, UV, Cream

## INTRODUCTION:

Ageing is a natural phenomenon that involves various changes in the skin's structure and function. One of the significant signs of ageing is the development of wrinkles, fine lines, and sagging skin. To counter these changes, anti-ageing creams are formulated using different natural and synthetic ingredients.[1] Pomegranate seed oil is a natural ingredient that has been used for various medicinal and cosmetic purposes. Pomegranate seed oil is rich in antioxidants, which can help protect the skin from damage caused by free radicals. Additionally, pomegranate seed oil has anti-inflammatory properties, which can help reduce inflammation in the skin.[2]

Skin ageing is a dermatological condition that worsens with age or exposure to UV rays if no therapy is taken. Extensive study is being done on this skin issue, which entails the development of unsightly, visible markings on the skin's surface as a result of the breakdown of cutaneous elastic fibres, which has a negative impact on cell function.[3]

The most visible organ, the skin, performs vital tasks including controlling body temperature and sensing pressure, temperature, and apin. It also serves as an essential barrier against pollution and other environmental effects, making ageing quite obvious. Thinning, sagging, the emergence of age spots and dry skin are all signs of ageing.[4]

Ageing can be divided into two categories: intrinsic ageing, which is a natural and inevitable process, and actinic ageing, which depends on a person's exposure to ultraviolet radiation. UV exposure causes a variety of skin changes, including wrinkles, sunburn, immune system suppression, cancer, and the earliest ageing of the skin.[5,6]

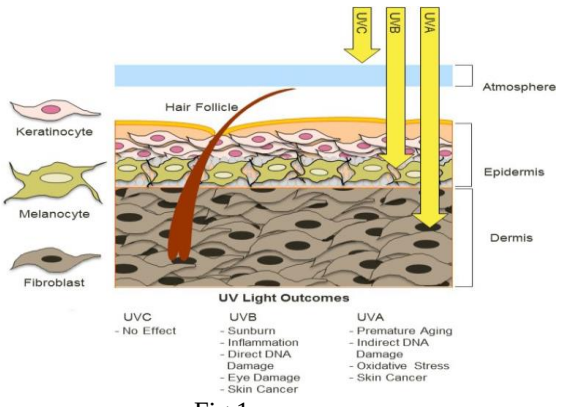



Fig 1

UVA and UVB energy make up the majority of the UV radiation found in ambient sunlight. Despite being extremely bioactive, UVC is not significantly absorbed by terrestrial organisms since the majority of it is by ozone. UVB can penetrate the epidermis and directly harm DNA. UVA has the ability to enter the dermis and raise ROS levels, which can cause DNA mutagenesis.[7]

## POMEGRANATE SEED OIL

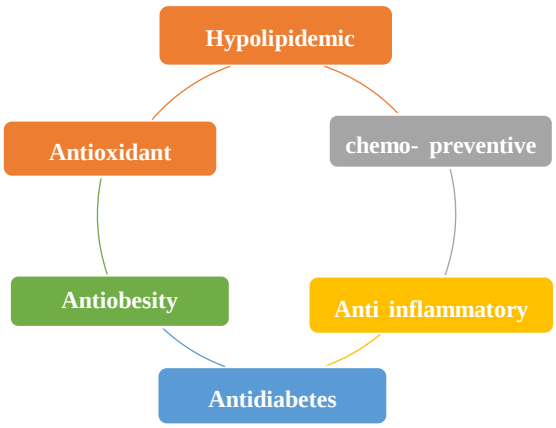
For thousands of years, the Punicaceae- family pomegranate has been utilised as a fruit medicine, pomegranate cultivation is most prevalent in the Mediterranean region, which includes Iran, India, and Pakistan. It is thought that the pomegranate was one of the first fruits to be domesticated for its health benefits, according to early bronze period excavations (3500-2000 BC). Pomegranates have been grown for their therapeutic benefits by humans for more than 4,000 years. Pomegranate juice, seeds, leaves, blossoms, bark and roots all have different effects. The most significant traditional applications of pomegranate are lowering fever, treating diabetes, anthelmintic, anti- diarrhoea, blood tonic, stopping the bleeding, and mending ulcers. Pomegranate seeds are an oil-rich by product of the juice industry.[8,9]

Punicic acid, the primary bioactive component of PSO, has been demonstrated to have powerful anti-oxidative properties that support its protective effects against a variety of diseases, including osteoporosis. Punicic acid is also anti-obesity, increases the expression of genes related to lipid metabolism and antioxidants, and modifies the structure and function of high-density lipoprotein (HDL).[9]

## CHEMICAL COMPOSITION

The chemical components of pomegranate seed oil extract (PSOE) were identified using gas chromatography, mass chromatography (GC-MS) and inductively coupled plasma-mass spectrometry (ICP-MS). Octadecenamide, tocopherol, oleamide, squalene, stigmas-3,5-diene, and other potentially beneficial phytochemical blends are among the substances in PSOE. The fruit of the pomegranate is made up of arils, which make up 40% of it, and seeds, which make up 10%. Pomegranate seeds have a variety of ingredients, including fatty acids and polyphenols, which contribute to their positive benefits. About 12% to 20% of the total weight of the seeds is made up of pomegranate seed oil (PSO). PSO includes 14 fatty acids, with punicic acid (50–80%) being the most prevalent. Linoleic acid (13-20%), palmitic acid (6–9%), stearic acid (2–3%), oleic acid (8–9%), linolenic acid (0.06-0.08%), and arachidic acid (0.68–0.90%) are the next most prevalent fatty acids.[10,11,13]

## PROPERTY OF POMEGRANATE SEED OIL-[10]



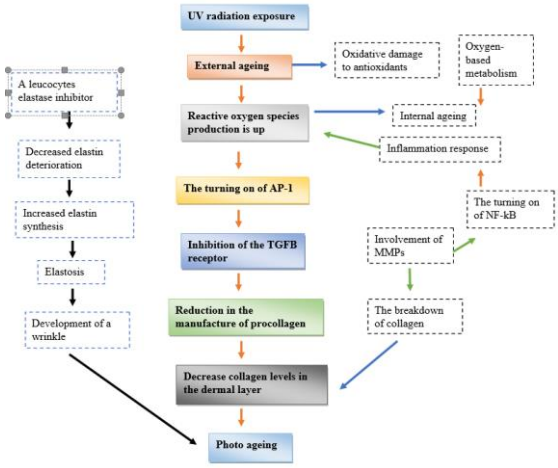




**FIGURE 1: Ageing Process Mechanism [13]**

**Table 1: Factors and effects of ageing[14]**

| S.N. | Causes | Non-visual impact | Visual impact |
|---|---|---|---|
| 1. | **Internal**: Genetic analysis of cellular, structural, and procedural elements hormonal changes, decreased bone density, and other | Decreased in collagen Decreased in elastin Decreased in Hyaluronic acid fat loss and bone resorption and dermal redistribution thinning | Fine folds and wrinkles slack eyelids dry skin, sunken cheeks, and jowls |
| 2. | **External**: Smoking face expressions, sleeping position, and gravity in a picture | Dermal thinning and epidermal thickening | Rough skin with wrinkles and creases, blemishes and pigmentation, and freckles |

## MATERIAL AND METHODS:

This study aimed to develop an anti-ageing cream using pomegranate seed oil as an active ingredient. The materials used in the cream included water, glycerin, stearic acid, emulsifying wax, pomegranate seed oil, Vitamin E oil, preservative, and essential oil. The cream was prepared using a double boiler and a hand mixer, and the pH was adjusted to between 4.5 and 5.5 for optimal effectiveness and stability. The cream was stored in a sterilized container and tested for stability over a 3–6-month period. The results showed that the cream was effective in reducing the signs of aging on the face and neck. The cream was well-tolerated by the subjects, and no adverse effects were reported. These findings suggest that the anti-aging cream using pomegranate oil has the potential to be an effective and safe cosmetic product.

## PREPARING THE BOTANICAL MATERIALS[15] (POMEGRANATE SEED'S OIL):

**Name of the plant:** Punica Granatum
**Kingdom:** Plantae (angiosperms)
**Order:** Myrtales
**Family:** Lythraceae
**Genus:** Punica
**Species:** Pgranatum
**Materials:**

**Cream formulation:** Took the stearic acid, cetyl alcohol, glycerine, petroleum jelly, methyl paraben, and pomegranate seeds oil, in a borosilicate glass breaker at 75˚C and maintain that heating temperatures (oil phase). In another beaker dissolve potassium hydroxide and methyl paraben in distilled water by maintaining temperatures 75˚C with electric heating mantle. Use a glass rod to stir the solution until the water phase is completely free of all solids. Gently pour the heated aqueous phase into the heated oily phase while continuing to mix. Until it creates a smooth cream, continues to mix using a glass rod. Add rose water as a fragrance after the cream is fully formed. Put this cream on the slap and, if necessary, add a few drops of distilled water. Then, mix the cream geometrically over the slap to give it a smooth texture and to thoroughly combine all the ingredients. Slap technique or extemporaneous cream preparation is the name of this technique.

### Extraction of pomegranate oil:

The extraction of pomegranate oil from their seeds that generally start by collecting fresh and ripe pomegranate fruits, Cut the fruit into halves or quarters, and then remove the seeds. Discard any damaged or discolored seeds. Thoroughly clean the seeds by rinsing them in water and then drying them with a clean towel or paper towel. Crush the cleaned seeds using a pestle and mortar or a seed oil press machine. Crushing the seeds can help to release the oil. If using a seed oil press machine, feed the crushed seeds into the machine and follow the manufacturer's instructions for extracting the oil. This method typically involves pressing the seeds under high pressure to extract the oil. If using the pestle and mortar method, transfer the crushed seeds to a cheesecloth or muslin cloth, and then squeeze the cloth to extract the oil. Once the oil is extracted, transfer it to a clean glass jar or bottle, and store it in a cool, dark place away from direct sunlight. You can also filter the oil to remove any seed residue or impurities by pouring it through a fine-mesh sieve or cheesecloth.[16,17]

Pomegranate oil extracted from seeds is rich in antioxidants, vitamins, and minerals that make it an excellent ingredient for skincare and hair care products.[17]

**Method:** Pomegranate seed oil is a valuable natural product that has gained attention for its health and cosmetic benefits. This study aimed to investigate the extraction of pomegranate oil from seeds using a seed oil press machine or pestle and mortar method. Fresh and ripe pomegranate fruits were collected, and the seeds were cleaned and crushed. The crushed seeds were then processed using a seed oil press machine or squeezed through a cheese cloth using the pestle and mortar method.

The oil was collected, filtered, and stored in a cool, dark place. The oil's chemical composition was analyzed using gas chromatography-mass spectrometry (GC-MS) to determine its fatty acid composition and antioxidant content. The results showed that the extraction of pomegranate oil from seeds using both methods was successful. The oil was found to be rich in fatty acids, such as punicic

acid and linolenic acid, and contained high levels of antioxidant compounds, including tocopherol and polyphenols. These findings suggest that pomegranate oil extracted from seeds is a valuable natural product that can be used in various applications, such as cosmetics, nutraceutical, and pharmaceuticals.[18] Begin by sterilizing all equipment and work surfaces that will come into contact with the cream to prevent contamination. Combine the stearic acid, emulsifying wax, and pomegranate oil in a heat-safe glass bowl or double boiler. Heat the mixture on low heat until it is fully melted. In another pot, heat the water and glycerin until they reach a temperature of 70-75°C. Once both mixtures have reached the desired temperature, slowly pour the water and glycerin mixture into the melted oil mixture while continuously stirring with a hand mixer or blender. Continue to mix the cream for 5-10 minutes until it becomes creamy and smooth. Add the Vitamin E oil and preservative to the cream and mix well. If desired, add 5 drops of essential oil of your choice and mix well. Check the pH of the cream with pH strips or a pH meter. The pH should be between 4.5 and 5.5 for optimal effectiveness and stability. Transfer the cream to a sterilized container and allow it to cool down to room temperature before using it. Store the cream in a cool, dry place away from direct sunlight and use within 3-6 months. That's it! Anti-aging cream using pomegranate oil is ready to use. Apply it to your face and neck before bed for best results

Various formulations are used to develop anti-aging creams using pomegranate oil. One of the simplest formulations is the use of pomegranate oil as a standalone ingredient. However, to enhance the efficacy of pomegranate oil, other natural ingredients can be added to the formulation. For example, Hyaluronic acid can be added to the formulation to increase the skin's hydration levels, which can help reduce the appearance of fine lines and wrinkles. Additionally, Vitamin C can be added to the formulation to increase collagen production, which can help improve skin elasticity.[19]

Another formulation that can be used to develop anti-ageing creams using pomegranate seed oil is the emulsion formulation. Emulsions are mixtures of oil and water, and they are commonly used in cosmetic formulations. To develop an emulsion formulation, pomegranate seed oil is mixed with water, emulsifiers, and other ingredients. The emulsifiers help to stabilize the mixture and prevent the oil and water from separating.

**Evaluation parameters of Anti-Ageing Cream:**

Various evaluation methods are used to test the efficacy of anti-ageing creams using pomegranate oil. One of the most common methods is the use of in vitro assays. In vitro assays involve testing the cream's efficacy in a laboratory setting. For example, the cream can be tested for its ability to reduce oxidative stress in skin cells using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay. Additionally, the cream can be tested for its ability to increase collagen production in skin cells using the hydroxyproline assay.[19]

Another evaluation method that can be used is the in vivo method. In vivo studies involve testing the cream's efficacy on human subjects. For example, the cream can be tested for its ability to reduce the appearance of fine lines and wrinkles using digital imaging techniques. Additionally, the cream can be tested for its ability to increase skin hydration levels using skin hydration measurements.

**Study of parameters:**

**Stability study:[20,21,22]**

A stability study of an anti-aging cream containing pomegranate oil should be conducted to ensure that the product remains safe, effective, and consistent throughout its shelf life.

The following are the general guidelines and steps involved in a stability study: Choose appropriate testing conditions:

The stability study should be conducted under various environmental conditions to mimic the potential storage and transportation conditions that the product may encounter during its shelf life. The testing conditions may include temperature, humidity, light exposure, and packaging materials.

**Set testing parameters:** Define the testing parameters such as the length of the study, the frequency of testing, and the analytical methods used to evaluate the product's stability.

**Test for physical stability:** Evaluate the cream's physical properties, such as color, odor, texture, and viscosity. These tests are important to identify any changes in the product's appearance, feel, and consistency.

**Test for chemical stability:** Analyze the chemical composition of the cream to ensure that the active ingredients and preservatives remain effective

and that no new chemical reactions or degradation products are formed. Microbial stability testing: Test the cream for the growth of bacteria, yeast, and Mold, which can cause spoilage and reduce the product's safety.

**Accelerated stability testing:** Conduct tests under accelerated conditions to simulate the product's aging process and evaluate its stability over a shorter period. This is done by exposing the product to higher temperatures and humidity levels than those encountered in normal storage conditions.

**Establish shelf life:** Based on the results of the stability study, establish the product's shelf life, which is the length of time that the product remains safe and effective under normal storage conditions.
In summary, a stability study of an anti-aging cream containing pomegranate oil is essential to ensure that the product remains safe, effective, and consistent throughout its shelf life. The study should include physical and chemical stability testing, microbial stability testing, and accelerated stability testing, among others, to establish the product's shelf life under various environmental conditions.

### Organoleptic study:[23,24,25]

Organoleptic study for herbal formulation is a sensory analysis that evaluates the sensory characteristics of a product using the human senses of sight, smell, taste, touch, and hearing. The Organoleptic evaluation of an anti-aging cream of pomegranate oil should be conducted using a scientific approach, including evaluating its appearance, odor, pH, viscosity, spreadability, skin feel, and stability. These tests will help ensure that the product is of high quality, safe, and effective for its intended use.
In the case of an anti-aging cream of pomegranate oil, the following organoleptic evaluation can be conducted in a scientific manner:

**Appearance:** Evaluate the cream's color, clarity, and texture. The color should be uniform and consistent, while the texture should be smooth and free of lumps or grittiness. Odor: Evaluate the cream's odor for its intensity, character, and stability. The odor should be pleasant and consistent throughout the product's shelf life.

**pH:** Measure the pH of the cream using a pH meter. The pH should be within the acceptable range for the product, typically between 4.5 and 6.5.

**Viscosity:** Measure the cream's viscosity using a viscometer. The viscosity should be appropriate for the product, allowing for easy application and absorption into the skin.

**Spreadibility:** Evaluate the cream's Spreadibility by measuring the area covered by a fixed amount of cream. The Spreadibility should be appropriate for the product, allowing for easy and even application on the skin.

**Skin feel:** Evaluate the cream's skin feel by applying it to the skin and observing its absorption rate, residual tackiness, and moisturization effect. The cream should be easily absorbed into the skin, leaving no greasiness or stickiness. Evaluate the cream's stability by observing any changes in its appearance, odor, pH, viscosity, or skin feel over time. The cream should remain stable throughout its shelf life, with no significant changes in its sensory characteristics.

**Table 2: Effect for developing older on age: (Joshi et al, 2013)[26]**

| S.N. | Age | Ageing issue | Noticeable outcome |
|---|---|---|---|
| 1. | 25-40 | A few sun rays a loss of collagen. Minimal fat loss certain vitamins for water loss stress | Upper face begins to develop frown lines, tiny traces midface wrinkles and folds start to develop |
| 2. | 40-55 | Increased solar damage greater loss of collagen greater fat loss supplementing water loss more | Upper face frown lines that are more distinct more noticeable fine lines, wrinkles, and creases in the middle of the face, along with some lip thinning and hollowing of the eyes and cheeks. |
| 3. | 55+ | Significant solar damage significant collagen loss significant weight-loss aids tension | Deep frown lines in the upper facial extension, as well as fine lines, wrinkles, and folds in the midface, are becoming more obvious. |

## CONCLUSION:

Pomegranate seeds oil include a variety of ingredients in varying proportions to achieve several effects on the skin, including skin whitening, anti-wrinkle, anti-ageing and sunscreen effects.
In conclusion, pomegranate oil is a natural ingredient that has been used for various medicinal and cosmetic purposes. The anti-ageing properties of pomegranate oil make it an excellent ingredient for the formulation of anti-ageing creams. Various formulations, including standalone formulations and emulsion formulations, can be used to develop anti-ageing creams using pomegranate oil. The efficacy of pomegranate oil-based anti-ageing creams can be evaluated.

## SUMMARY:

One of the most significant environmental health risks is UV radiation, which is obviously responsible for age-related skin changes such wrinkles, pigmentary changes, thinning, and carcinogenesis. Due to complicated sociocultural circumstances, indoor tanning and other vocational and recreational activities may actually result in more UV exposure. The skin is the most visible and, hence, most susceptible portion of the body to damage. Topical treatments, such as creams, are preferred for cuts, bruises, and other minor ailments. Topical phrasings provide some advantages over other conventional systems, including convenience of use, a lesser risk of unwanted side effects, a non-invasive method, and improved patient compliance.

Punicic acid has been shown to protect the skin's collagen fibers, hastening wound healing and lessening the visibility of scars.

Punicic acid's anti-inflammatory properties have successfully treated skin conditions like eczema and psoriasis.

An effective anti-aging substance is pomegranate oil. Antioxidants, such as vitamins A (retinol) and C (ascorbic acid), serve to fend off free radicals while smoothing out wrinkles and fine lines.

The focus of the current study is on the potential of herbal extracts for cosmetic applications. The personal care industry has greatly expanded its usage of cosmetics. The usage of bioactive substances in cosmetics affects how biologically the skin functions and supplies the nutrients needed for healthy skin. Throughout the study period, the produced formulations shown high consistency, no sign of phase separation, and good Spreadibility, There was any discernible change in the formulations' visual appearance, character, or aroma during the study period, according to stability measures.

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Research Article

# FORMULATION AND EVALUATION OF HERBAL ANTI-AGEING CREAM CONTAINING POMEGRANATE SEED OIL

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**ABSTRACT:**

Skin is the most exposed organ of the body, is crucial for establishing social bonds and defending against environmental harm. Dermatologist and cosmetic concerns about skin ageing are growing quickly as our society's ageing population grows. Cell death is brought on by oxidative stress, which also causes protein denaturation, lipid per oxidation, and intracellular DNA damage. This study evaluated the anti- wrinkle effects of pomegranate seed oil using a photo aged hairless rat model. The research article also discussed the evaluation methods used to test the efficacy of pomegranate seed oil-based anti-ageing creams. The results of the studies suggest that pomegranate seed oil-based anti-ageing creams can be effective in reducing the signs of ageing. Data shows that the anti-ageing cream (anti wrinkle) treatment greatly improved skin condition of rat suffering from UVB-induced photo ageing , based on the parameters including the skin erythema index, wrinkle area measurement, allergic response, skin texture. The goal of the research was to develop anti ageing cream for decreased ageing, photo ageing, and provide moisturizing, nourishing, whitening, and treating various skin diseases.

**Keywords:** Cosmetics, pomegranate seeds oil, extrinsic skin ageing, photo ageing, rat models.

## INTRODUCTION:

The face is exposed to sunlight continuously from birth, causing the skin to progressively accumulate damage that causes obvious indications of aging to occur by marking specific areas of the skin or recurring facial expressions. Continuous UV exposure can also cause various changes that are classified as photo-induced damages, including vascular homogeneities and pigmentation loss, elasticity loss in the skin, and texture deterioration (elastosis, hyperkeratosis, and yellowing). [1]

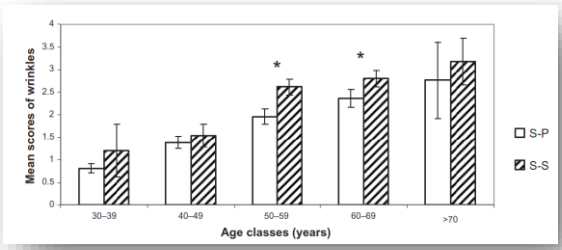
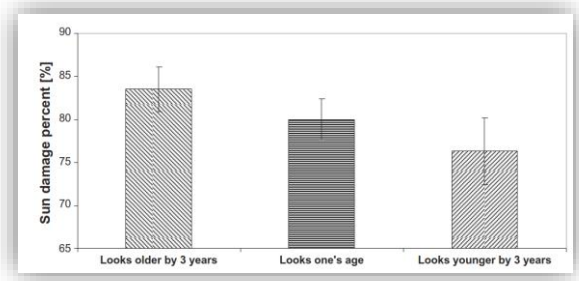



Fig- 1
S-P means Sun Phobic and S-P means Sun Seeking




From the Above figure-1 it shows that In Australian women have the higher number of aging as compared to USA, UK and Canada. The reason of aging is due to the UV exposure, it happens due to geographical location of the Australia is southern hemisphere and northern tip of Australia is closer to equator region due to which it is higher prone to direct exposure to sun and the greatest differences were seen between Australian and US women, the Australian and US women, the Australian women reporting some signs of advanced ageing approximately 20 years earlier than those from the USA.[2]

One of the main indicators of physical aging is aging of the skin. The aging process of the skin is influenced by hormone fluctuations, metabolic processes, genetics, and environmental exposure. Therefore, it is thought that the main contributors to skin aging are intrinsic and extrinsic damage. The

skin uses a range of natural antioxidants to guard against damage caused by free radicals.[3]

The word "cosmetics" comes from the Greek word "cosmetics," which meaning "to adorn." In the past, "cosmetics" was the term for any substance intended to enhance and beautify appearance. Humanity has always needed to take care of its skin. Although elegant, smooth skin is a sign of vitality, the flawless appearance is actually the result of an underlying protein called collagen. Collagen acts as a wonderful cushion to maintain skin smooth and stiff while framing an even layer beneath the skin. As we become older, fine wrinkles start to appear. It is an inevitable part of the regular aging process; nevertheless, premature maturing is caused by excessive sun exposure, tobacco smoking, and dehydration. With the right defensive measures, the aging process can be slowed down considerably.[4]

The World Health Organization (WHO) and our nation have been supporting traditional medicine because it is more affordable, widely accessible, and thorough—especially in developing nations. It's also true that 8% of people on the planet receive their primary medical care from medicinal plants. The developed world, along with its citizens, acknowledged the value of traditional medicine and established protocols, guidelines, and treatment standards for ethnomedicine.[5]

One of the first edible fruits, the pomegranate (Punica granatum L.), is a member of the Punicaceae family and has been utilized widely in folk medicine across many civilizations. This fruit is indigenous to Iran, where it is produced extensively along with India, the United States, and other near and far eastern countries. An estimated 1,500,000 tons of this crop are produced globally, with 47% of that amount coming from Iran, which has the largest area under cultivation.[6]

Pomegranates are rich in lipids such as oleic acid, stearic acid, and palmitic acid as well as polyunsaturated fatty acids like linoleic and linolenic acid.[7]

PSO accounts about 12–20% of the overall weight of seeds. About 80% of the contents of seeds are made up of conjugated octadecatrienoic fatty acids, and PSO is thought to be a rich source of these fatty acids, especially punicic acid (PA) (cis9, trans11, cis13 acid), which is the primary fatty acid among them. Pomegranate juice, peels, leaves, and flowers all have strong antioxidant qualities, however the juice, peel, and oil all have mildly estrogenic effects. Pomegranate seeds contain a high amount of conjugated α-linolenic acids (CLn) and ethnomedical indications. Numerous pharmacological effects are associated with pomegranate seed oil (PSO), which has a high concentration of punicic acid (PA), a conjugated isoenolenic acid isomer. Antioxidant, anti-inflammatory, nephroprotective, hepatoprotective, neuroprotective, anti-cancer, strengthening the immune system, improving carbohydrate metabolism, and lowering insulin resistance are some of its primary characteristics.[8]

## MATERIALS AND METHODS

## MATERIALS

The materials used in this study were pomegranate seeds oil, aloe vera gel, vitamin E, turmeric powder, stearic acid, cetyl alcohol, glycerine, petroleum jelly, methyl paraben, potassium hydroxide, rose water, distilled water. Aloe vera, turmeric, and vitamin E capsule were collected from the local market in Bhopal MP.

### Cream formulation

Took the stearic acid, cetyl alcohol, glycerine, petroleum jelly, methyl paraben, and pomegranate seeds oil, in a borosilicate glass breaker at 75˚C and maintain that heating temperatures (oil phase). In other beaker, dissolve potassium hydroxide and methyl paraben in distilled water by maintaining temperatures 75˚C with electric heating mantle. Use a glass rod to stir the solution until the water phase is completely free of all solids. Gently pour the heated aqueous phase into the heated oily phase while continuing to mix. Until it creates a smooth cream, the continues to mix using a glass rod. Add rose water as a fragrance after the cream is fully formed. Put this cream on the slap and, if necessary, add a few drops of distilled water. Then, mix the cream geometrically over the slap to give it a smooth texture and to thoroughly combine all the ingredients. Slap technique or extemporaneous cream preparation is the name of this technique.

**Figure 2 Images of formulated cream**

| S. No | Ingredients | F1 | F2 | F3 | F4 | F5 | F6 |
|---|---|---|---|---|---|---|---|
| 1 | PSO | 2ml | 1ml | 3ml | 5ml | 7ml | 8ml |
| 2 | Aloe Vera extract | 2ml | 2ml | 2ml | 3ml | 3ml | 2ml |
| 3 | Turmeric extract | 1ml | 1ml | 1ml | 2ml | 2ml | 1ml |
| 4 | Vitamin E | 1ml | 1ml | 1ml | 2ml | 2ml | 1ml |
| 5 | Stearic acid | 2gm | 2gm | 0.5gm | 10gm | 15gm | 12gm |
| 6 | Cetyl alcohol | 1gm | 1gm | 1gm | 5gm | 5gm | 3gm |
| 7 | Glycerine | 1ml | 1ml | 1gm | 5ml | 5ml | 3ml |
| 8 | Petroleum jelly | 1gm | 1gm | 1gm | 5gm | 5gm | 3gm |
| 9 | Methyl paraben | 0.5mg | 0.5gm | 0.5gm | 2.5gm | 2.5gm | 2gm |
| 10 | Potassium hydroxide | 0.5gm | 1gm | 0.5gm | 2.5gm | 2.5gm | 2gm |
| 11 | Distilled water | qs | qs | qs | qs | qs | qs |
| 12 | Rose water | qs | qs | qs | qs | qs | qs |

**Table 1: Formulations of anti-ageing cream**

## Evaluation parameters of Anti-Ageing Cream:

Various evaluation methods are used to test the efficacy of anti-ageing creams using pomegranate oil. One of the most common methods is the use of in vitro assays. In vitro assays involve testing the cream's efficacy in a laboratory setting. For example, the cream can be tested for its ability to reduce oxidative stress in skin cells using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay. Additionally, the cream can be tested for its ability to increase collagen production in skin cells using the hydroxyproline assay.[9]

Another evaluation method that can be used is the in vivo method. In vivo studies involve testing the cream's efficacy on human subjects. For example, the cream can be tested for its ability to reduce the appearance of fine lines and wrinkles using digital imaging techniques. Additionally, the cream can be tested for its ability to increase skin hydration levels using skin hydration measurements.

## Organoleptic study:[10,11,12]

Organoleptic study for herbal formulation is a sensory analysis that evaluates the sensory characteristics of a product using the human senses of sight, smell, touch. The Organoleptic evaluation of an anti-aging cream of pomegranate oil should be conducted using a scientific approach, including evaluating its appearance, odor, pH, viscosity, Spreadibility, homogeneity, skin feel, removal, irritancy test, and stability. These tests will help ensure that the product is of high quality, safe, and effective for its intended use.[10]

In the case of an anti-aging cream of pomegranate oil, the following Organoleptic evaluation can be conducted in a scientific manner:

**Appearance:** Evaluate the cream's color, clarity, and texture. The color should be uniform and consistent, while the texture should be smooth and free of lumps or grittiness. Odor: Evaluate the cream's odor for its intensity, character, and stability. The odor should be pleasant and consistent throughout the product's shelf life.

**After feel:** We measured the amount of emollient, slipperiness, and thickness residue that remained after applying a specific amount of cream.

**Removal:** It was discovered how quickly the cream could be removed by running tap water over the area where it was applied.

**Irritancy test:** The Cream was applied to the left hand's specific area, and the time was recorded. Oedema, skin redness, and irritability were monitored up to a 24-hour period at regular intervals.

**Grittiness:** On a glass slide, a tiny bit of cream was put, and the surface was then illuminated to look for any foreign particles.

**Table 2: Organoleptic activity**

| Sl. No. | Specification | Limits |
|---|---|---|
| 1 | State | Semisolid |
| 2 | Color | Yellowish white, white |
| 3 | Odor | Characteristic |
| 4 | Texture | Smooth |

## RESULTS AND DISCUSSION

**pH:** Measure the pH of the cream using a pH meter. In order to calibrate the pH meter, standard buffer solution was used. 0.5g of weighted cream that had been dissolved in 20.0 ml of distilled water and its pH was tested.[11] The pH should be within the acceptable range for the product, typically between 4.5 and 6.5. The formulation's pH was tested at 1, 10, 30, 60 and 90 days after preparation. The results of this research are shown in table number 3.

**Table 3: pH observation for various time periods**

| Temperature | Initial pH | pH after 1 month | pH after 2 month | pH after 3 month |
|---|---|---|---|---|
| 37±1 ˚C | 6.80 ± 0.01 | 6.50 ± 0.04 | 6.30 ± 0.03 | 5.80 ± 0.02 |

### Determination of type of cream:

In this experiment, the cream was diluted with either water or oil. Water is the dispersion medium, thus if the cream is diluted with water and remains stable, it is an o/w type cream of cream. However, if the cream is diluted with oil, the cream will break since oil and water are not miscible.[13] In the present study, 2.5 grammes of cream were taken, and the cream was gradually diluted with distilled water.

**Figure 3 Dilution test**

**Viscocity:** The viscosity of the cream was measured using a Brookfield viscometer DV-II + Pro (Brookfield engineering laboratories) with cylinder spindle #64, Test samples were collected in 250ml beakers that were clean and dry, and the viscosity of each sample was assessed using the viscometer's regular operating methods. The reading was recording at100% torque. Sample temperatures were 37±1˚C. We read the value in centipoises. The viscosities of formulated anti-ageing creams was found in the range of 3260 to 6499 Cp and it was closure to the standard marketed cream, it indicate that sufficient amount of oil phase and aqueous phase was used during formulation of cream. The results are given in table number 4.

**Spreadibility study of cream:** A glass device put up in the lab was used to assess the Spreadibility of the cream formulation. The cream emulsion was sandwiched between the two glass slides. A 500 gm mass was then placed on the slide for 1 minute to compress the sample and create a consistent thickness. Extra cream was then scraped off. Spreadibility is calculated using the formula:

**Formula of Spreadibility: S = M x L / T**

Where, M is the weight that has been put to the top slide, L is the size of the glass slide, and T is the number of seconds.[14] The Spreadibility was found to range about 21 and 30 gm.cm/sec. it was found to be within the Spreadibility range of commercial cream, The cream's formulation made it simple to distribute without creating a lot of friction, the results are given in table number 4.

**Microstructure observation:** An optical microscope with a 40x magnification was used to analyse the morphology of prepared cream. Before the microscopic examination, a cover slip was placed over the 1gm of cream samples, which had been smeared gently over the slide. The slide was placed on a microscope slide. Photomicrography picture of the emulsion was captured and it was evident that oil globules were present on the continuous water phase, which proves that the anti ageing (Pomegranate seeds oil) cream was properly manufactured.

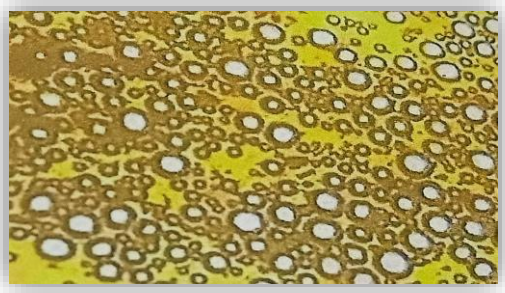


**Fig 4: Microscopic structure of cream**

**Table 4: Cream formulation and their results:**

| Formulations | pH | Viscosity(cP) | Spread ability(gm*cm/sec) | Sensitivity | Erythema | Phase separation | Wash ability |
|---|---|---|---|---|---|---|---|
| F1 | 6.80 | 7558 ± 1.02 | 21.6 | No irritation | Nil | Not phase separation | Easily washable |
| F2 | 6.00 | 8698 ± 1.00 | 22.5 | No irritation | Nil | Not phase separation | Easily washable |
| F3 | 6.50 | 6839 ± 1.22 | 20.8 | No irritation | Nil | Not phase separation | Easily washable |
| F4 | 6.32 | 5639 ± 2.51 | 26.6 | No irritation | Nil | Not phase separation | Easily washable |
| F5 | 6.26 | 4829 ± 1.33 | 25 | No irritation | Nil | Not phase separation | Easily washable |
| F6 | 7.00 | 4457 ± 1.15 | 24.1 | No irritation | Nil | Not phase separation | Easily washable |

## STABILITY STUDY OF FORMULATION[15]

Final formulations including active components were kept in plastic containers at 2 to 4˚C, 25˚C and 40˚C. After week 4, all formulations physiochemical characteristics were assessed to determine their physical stability.

The optimised formulation was stored in an airtight container at the specified temperature to gauge the stability of the cream of pomegranate seeds oil. The measurement used for evaluating the stability was determined based on organoleptic properties, pH, and viscosity. At regular intervals of time (0, 1, 2, and 3 months), samples of the pomegranate seeds oil cream were taken and every evaluation parameters was recorded. The results of the stability study are given in the following table number 4.

**Table 4: Data of stability study**

| Temperature | Homogeneity | Phase separation | Simple removal |
|---|---|---|---|
| 2-4˚C | Homogeneous | No | Remove quickly |
| Room temperature | Homogeneous | No | Remove quickly |
| 40˚C | Slightly liquefying | No | Remove quickly |

**Table 5: Accelerated stability study**

| Months / Test | Anti-ageing cream | | |
|---|---|---|---|
| | Initial month | After two month | After three month |
| **Physical features** | Semi solid | Semi solid | Semi solid |
| **Texture** | Good | Good | Good |
| **Odour** | Characteristic | Characteristic | Characteristic |
| **Thermal stability** | Ok | Ok | Ok |
| **Deterioration of goods** | Nil | Nil | Nil |



## IN VIVO EVALUATION OF FORMULATED ANTI-AGEING CREAM:

Both sexes of albino rats (weighing 150–180g) will be used in the studies. The animals must be kept in groups of six in polyacrylic cages measuring 38 by 23 by 10 cm, and they must be kept in a typical laboratory environment with a temperature of 25 °C, a dark/light cycle, and relative humidity between 60 and 70 %. They will consume a pellet diet along with water additives. The animals will become accustomed to the laboratory environment for seven days before the studies begin. Animal research was done at the pharmacology division. Truba institute of Pharmacy, Bhopal (M.P.) with due permission from Institutional Animal Ethical Committee(IAEC approval no. PH/IAEC/TIP/2023), all the research was performed according to the animal ethics committee guidelines for the experimental animals.

**Selection of animal model:**[16]
There are six animals in each of the four groups into which the animals were divided.

Group 1 will be designated as the standard control.

Group 2 will serve as the negative control. (Ageing induced)

Group-3 will be named as marketed control and ageing will be treated with marketed anti-ageing cream.

Group-4 will be assigned as test groups that will treated with formulated cream

**Procedure to develop the ageing:** All the animals were anesthetized by chloroform (5ml), after shaving; a hair removal cream was used to completely remove the hair, prepare the ageing induced assembly, and then it will keep under for exposing UV radiation (UVB radiation 320-290nm). This process will take place for 7-10 days, after this process wrinkle develop and the formulated cream and marketed cream was applied regular to all animals for 30 days.

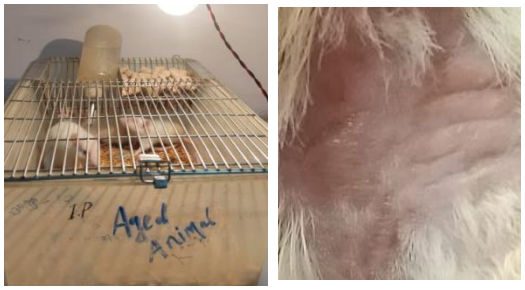



Fig5. Induced ageing

## Evaluation parameters:[17]

- Area of skin wrinkles.
- Skin irritation study.
- Photographic comparison.
- Skin texture.
- Allergic response.

**1. Area of skin wrinkle-** The wrinkle reduced property was evaluated by measuring the area of wrinkle alternatively before applying the cream. The length of the ageing was measured using a scale and transparent paper by placing the paper on ageing and tracing it out on alternate day. Significant decrease in area of the ageing (around 0.33 mm in every 5$^{th}$ day) in the test group of animals as compare with the marketed and negative control groups animal, it indicates that formulated cream is effective for ageing treatment, the area of ageing in test group decreases enough to justify the effectiveness of the formulated cream of pomegranate seed oil.

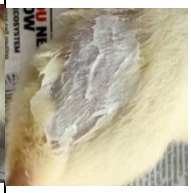
**Table- 6 Area of skin wrinkle**

| Animal group | 0$^{th}$ day | 5$^{th}$ day | 10$^{th}$ day | 15$^{th}$ day | 20$^{th}$ day | 25$^{th}$ day | 30$^{th}$ day | 35$^{th}$ day |
|---|---|---|---|---|---|---|---|---|
| Negative control | 1.5cm | 1.5 cm | 1.4 cm | 1.4 cm | 1.4 cm | 1.3 cm | 1.2 cm | 1.1 cm |
| Standard | 1.5cm | 1.1 cm | 0.7 cm | 0.3 cm | 0.2 cm | - | - | - |
| Test | 1.5cm | 1.3 cm | 0.8 cm | 0.5 cm | 0.2 cm | 0.2 cm | - | - |

**Table7: skin irritancy scoring table**

| Score | Reaction |
|---|---|
| 0 | No |
| 1 | Slightly |
| 2 | Moderate |
| 3 | Severe |

**Fig 6: Animal were used to evaluate skin irritancy(F5)**

| Remove hair | Apply cream | No skin irritation |
|---|---|---|
|  |  |  |

**3. Allergic response-** The symptoms allergic response includes rash, redness, swelling, cracked skin, and itching. When conducting the study, these elements were considered. Four animals in all were used in the investigation. Dorsal skin hair was removed using hair removal cream the formulated cream was applied on 1.5cm skin area for 10 days. On the basis of a scoring table, it was appraised. They are indicated by table number 8. The allergic response study's final finding were noted and reported in table number 8.

**Table 8: Allergic response**

| Score | Allergic symptoms | Reaction |
|---|---|---|
| 0 | Rash | No |
| 1 | Redness | Slightly |
| 2 | Swelling | No |
| 3 | Cracked skin | No |
| 4 | Itching | Moderate |

**4. Photographic comparison**

After creating an ageing according to the guidelines of the CPCSEA, photographs of each group of animal's ageing part were taken for the visual comparison, and the same is shown in figure7: Following formulation applied to the ageing each group of animals.

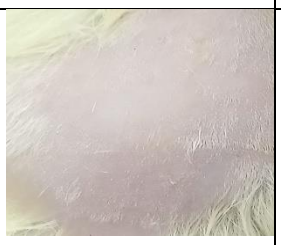
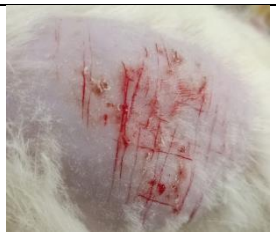
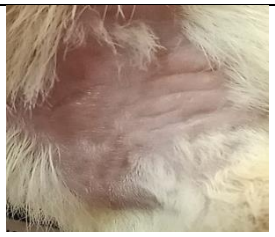
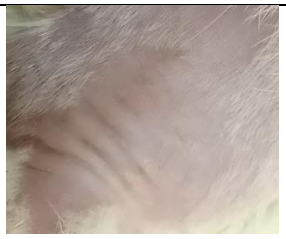
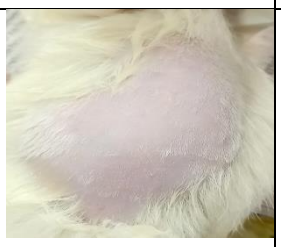
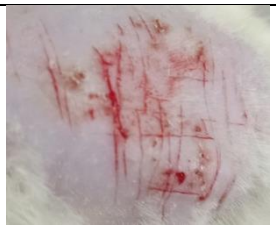
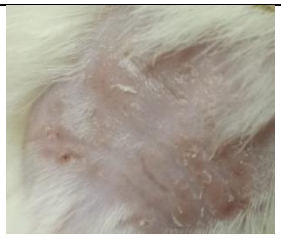
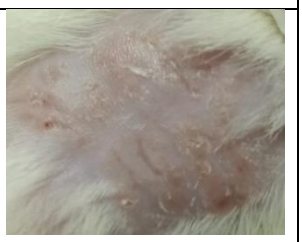
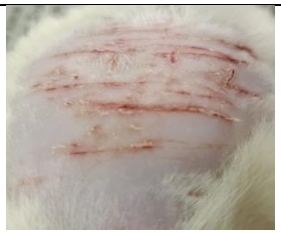
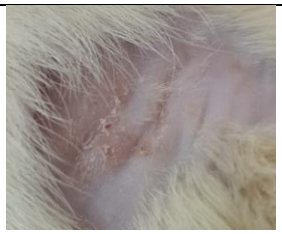
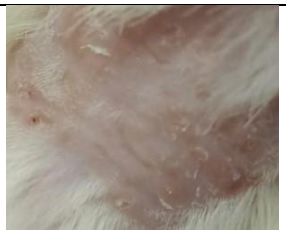
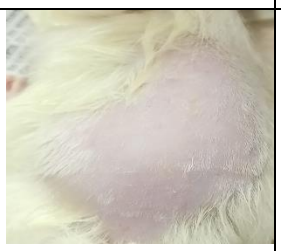
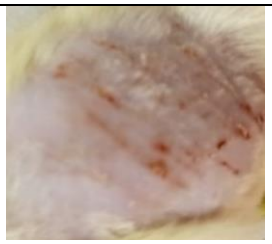
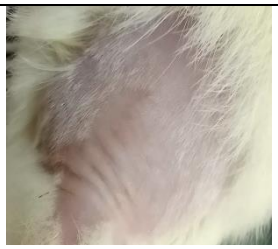
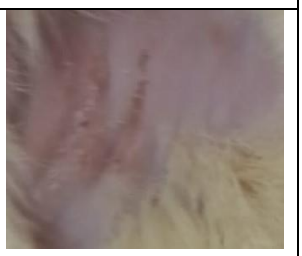
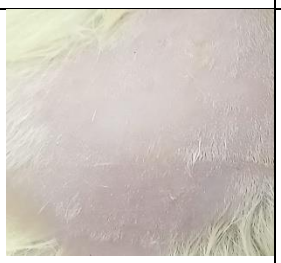
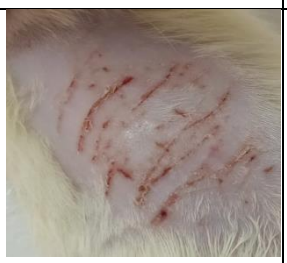
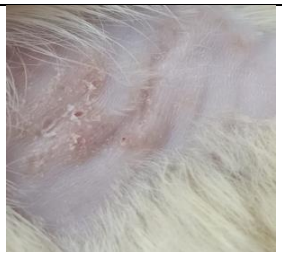
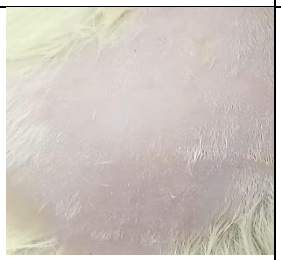
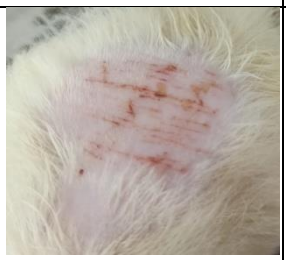
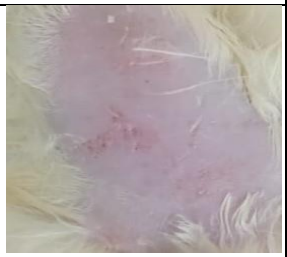
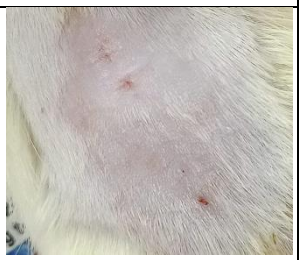
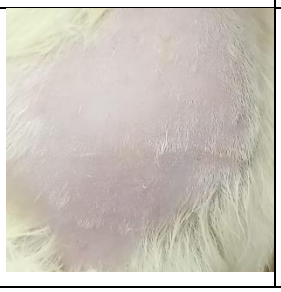
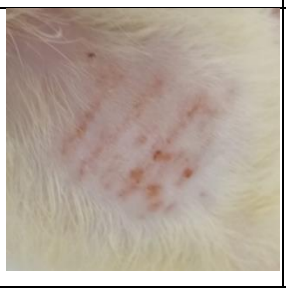
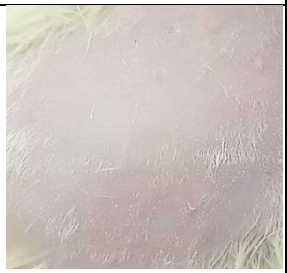
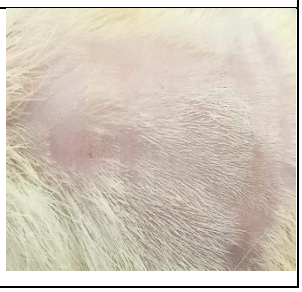
| Day | First Group | Second Group | Third Group | Forth Group |
|---|---|---|---|---|
| 0 |  |  |  |  |
| 5 |  |  |  |  |
| 10 |  |  |  |  |
| 15 |  |  |  |  |
| 20 |  |  |  |  |
| S25 |  |  |  |  |
| 30 |  |  |  |  |

Fig:7-Top-view images of ageing on days 0, 5, 10, 15, 20, 25, and 30 Where - Group 1 is the control group, Group 2 is the negative control group(induced ageing by uv light after 10 days we can follow the group3), Group 3 is the marketing group, and Group 4 is the test group

## *IN VIVO* STUDY

**1. Area of skin wrinkles-** The wrinkle reduced property was evaluated by measuring the area of wrinkle alternatively before applying the cream. The length of the ageing was measured using a scale and transparent paper by placing the paper on ageing and tracing it out on alternate day. Significant decrease in area of the ageing (around 0.33 mm in every $5^{th}$ day) in the test group of animals as compare with the marketed and negative control groups animal, it indicates that formulated cream is effective for ageing treatment, the area of ageing in test group decreases enough to justify the effectiveness of the formulated cream of pomegranate seed oil.

**2. Study on skin irritation** - The symptoms of rashes on skin studied includes Redness, itching, oedema, discomfort, and sensitivity. When conducting the study, these elements were considered. Four animals in all were used in the investigation. Dorsal skin hair was removed using hair removal cream and the formulated cream was applied for 10 days. On the basis of a scoring table, it was appraised. They are indicated by table number13. The skin sensitivity study's final finding were noted and reported in table number 13.

**3. Allergic response-** The symptoms allergic response includes rash, redness, swelling, cracked skin, and itching. When conducting the study, these elements were considered. Four animals in all were used in the investigation. Dorsal skin hair was removed using hair removal cream the formulated cream was applied on 1.5cm skin area for 10 days. On the basis of a scoring table, it was appraised. They are indicated by table number 15. The allergic response study's final finding were noted and reported in table number 15.

**4. Photographic observation and comparison-** After creating a ageing according to the guidelines of the CPCSEA, the images was captured of each animal groups for the visual comparison, and those image was attached in figure number.. It was observed that anti-ageing formulated cream of pomegranate seed oil showed nearly similar ageing healing as compared to the marketed anti-ageing cream. The ageing of test group animals marketed control group animals was healed completely on the $30^{th}$ day, and the ageing of negative control group animals was not healed till the last day of study.

A comparative study of marketed and formulated anti-ageing cream, after performing all the evaluation parameters, the comparison are given in table number9.

**Table 9: Comparison between marketed and formulated anti-ageing cream**

| Sl. No. | Marketed cream | Formulated cream |
|---|---|---|
| 1 | It is polyherbal formulation | It is single herb used |
| 2 | It is causes mild irritation after applying on skin | No irritation on skin |
| 3 | Need to apply 2-4 times a day | Two times a day |
| 4 | This is high cost cream | Low cost cream |
| 5 | Need at least 2 month for new ageing and takes 8 months to complete healing of old ageing | It is expected to take 2 month for new ageing |

## Conclusion

Our work's objective was to create, improve, and assess an anti-aging cream that included pomegranate seed oil, it includes ageing that are formed on our skin during the natural healing process of body cells. Ageing are developed in our body, during UV radiation, sunburn and environment pollution in our skin the immune system and natural healing process of our body activates immediately and send messages to form fresh collagen fibres and attack the infection. This results into the developments of ageing.

Vanishing cream of pomegranate seed oil was ready successfully using several substances, including potassium hydroxide, cetyl alcohol, and stearic acid, glycerine, perfume water and anti-microbial agents, The reason vanishing cream was chosen is that it left a thin coating on the skin that lets the cream stay on the skin longer, which ultimately results within significant reduction of ageing. In the study oil-in-water cream formulation was selected because They consist of tiny oil droplets scattered throughout a continuous water phase and the proposed cream

formulation would be more comfortable and cosmetically for skin ageing as It is easier to remove with water and less oily.

The prepared cream formulation was analysed for different in-vitro and in-vivo parameters such as Organoleptic parameters, types of emulsion test, viscosity and Spreadibility for in vitro and area of skin wrinkles, skin irritation, allergic response, skin texture and photographic comparison for in-vivo evaluation and stability study was also performed. The range of 3260 to 6499 Cp was discovered to be the viscosity of the formulated cream. The Spreadibility was found in the range of 21to 30 gm.cm/sec, pH was recorded at 6.5 constantly for 3 months which shows the stability of the cream.

In the animal study, healthy albino rats (150-300g) were chosen to perform every parameters of in-vivo research. Study was performed at Truba institute of Pharmacy, Bhopal (M.P.) in division of pharmacology lab with appropriate institutional authorization Animal Ethical Committee( IAEC approval no. PH/IAEC/2K23). An in-vivo study's findings showed that the ageing regulated by formulated pomegranate seed oil cream, recovery 100% with each better skin appearance and the ageing of test group was healed completely on the $30^{th}$ Dy. It was observed that formulated cream of pomegranate seed oil showed nearly similar ageing healing as compared to the marketed anti-ageing cream.

After performing different in-vitro, in-vivo and stability study parameters, it was observed that pomegranate seed oil was effective as a cream formulation to treat the skin ageing, skin wrinkles, fine line, dark spots and it also significant effectiveness against sunburn. Results of the study suggest that the formulated anti-ageing cream of pomegranate seed oil and its oil was safe, stable and cost effective for topical cosmetic formulation.

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Review Article

# Regulating E-Pharmacy Sales in India

**Sree Krishna Bharadwaj**

## ABSTRACT

Frequent adverts in periodicals and digital platforms encourage readers to acquire medications online by submitting doctor's prescriptions. Although this definitely reduces time and effort, most consumers of these online pharmacies are likely to be concerned about the authenticity, shelf life, and origin of the drugs that are being given. Currently, these internet-based pharmacies or e-pharmacy platforms function as an online marketplace or as an inventory model in accordance with the Information Technology Act, 2000 and the e-commerce regulations. This paper tries to analyse the present laws regulating e-pharmacies in India and the negatives of e-pharmacy in India.

**Key words:** e-pharmacy, law, online, regulation, drugs

## INTRODUCTION:

E-pharmacies, generally, employ three distinct types of business strategies. The inventory model, in which e-pharmacies own medicinal products and offer them directly to consumers via their online store or mobile app; the marketplace approach, in which e-pharmacies act as both a platform and a middleman, connecting consumers with physical drugstores; and the hybrid strategy, which is a blend of both of these. Netmeds, Tata1mg, Medlife, and PharmEasy are a few illustrations of internet pharmacy (Rao, 2023).

Laws regulating e-pharmacies

The Drugs and Cosmetics Act, 1940 ("D&C Act"), along with the Drugs and Cosmetics Rules, 1945 ("D&C Rules"), and the Pharmacy Act, 1948 are the principal pieces of law controlling the manufacturing, sale, and dissemination of medications and cosmetics in India at the moment (Nilanjan Sen, 2023). Several measures in the D&C Act and Rules assure the standards and grade of the pharmaceuticals. Importantly, no one is allowed to produce for selling or distribution, (i) any pharmaceutical product other than under and in compliance with the terms of an issued permit, and/or (ii) any substance that is contaminated, mis-branded, fake, or of a low standard.

If the aforementioned provisions are broken, there may be financial fines and jail time as penalties. In particular, retail sales of the medications listed in various Schedules of the D&C Rules are permitted only upon proof of and compliance with a prescription issued by a licenced medical professional. Furthermore, medication can be dispensed only by a licenced chemist upon valid prescription from a licenced physician.

The Pharmacy Act 1948 was enacted with the objective "to regulate the profession of pharmacy" (India, 2023). The Office of Drugs Controller General issued a notice to the drug controllers in the states and union territories in December 2015. In that notice, it was stated that the D&C Rules would still apply to drug sales that occur online and offline and that compliance with the rules would be required in both cases. In essence, the notice made it possible to provide licences for online pharmacies as well (Musyuni, 2023).

### Laws governing e-pharmacies in India

A draft amendment by *the Ministry of Health and Family Welfare vide its notification G.S.R. 817 (E) dated August 28, 2018* to the 1945 Drugs and Cosmetics Rules was released by the Ministry. The "sale of drugs by E-Pharmacy" chapter is proposed to be included in the rules. The word "e-pharmacy" has been added for the first time in the draft regulations, and it is defined as the business of distributing, selling, storing, exhibiting, or offering for sale pharmaceuticals through a web-based platform or any other digital medium. "Sale by way of e-pharmacy" refers to the selling of pharmaceuticals to hospitals, dispensaries, medical, educational, or research institutes, as well as to any other individual via retail sales conducted through e-pharmacy (Gupta, 2023).

Terms were additionally established for the procedure for applying and the validity of registration, as well as obligations placed on e-pharmacies which must be met in order to be registered, such as location, release of certain data, distribution and marketing procedures, etc. E-pharmacies are subject to certain limitations, such as the inability to promote their drugs for any purpose on TV, radio, online, in printed form, or any other form of media and special restriction has been placed on dealing in narcotic and psychotropic drugs as defined by the Narcotic Drugs and Psychotropic Substances Act, 1985, including tranquillizers, and drugs listed in Schedules of the Rules is prohibited. A mechanism for monitoring e-pharmacy and resolving complaints has also been put in place. In addition to the Consumer Protection Act of 2019, this mechanism gives people the ability to file a

complaint with the state drugs controller, if they suspect that sub-standard quality, fake, or counterfeited drugs are being supplied through e-pharmacy (Kartik Ganapathy, 2023).

Apart from to the aforementioned, e-pharmacies and its site are subject to the provisions of the IT Act and its regulations besides the Consumer Protection (E-Commerce) Rules, 2020 ("E-Commerce Rules"). While the E-Commerce Rules provide a comprehensive list of responsibilities for e-commerce entities to comply with, in addition to the details that must be announced in the website, the IT Act and its regulations set forth the rules and standards for operating a web-portal.

## Drawback in the proposed amendment

Although the proposed rules are a positive move, they fall short of meeting the challenges associated with operating internet pharmacies. The problem of outlawing internet pharmacies is one that many nations are grappling with as these businesses provide clients illicit medications in uncontrolled quantities without a valid prescription, sometimes in subpar or prohibited forms. Because these websites function covertly, it is very challenging to identify them and hold them accountable. Furthermore, the draft rules only provide for periodic inspections of pharmacies that are already registered and licence termination if standards are not followed.

The proposed Rules do not impose any obligation on websites that are not authentic, nor do they offer a method to deal with them. The legislators need to create a special department or give the Drugs Controller General of India more authority in order to: (1) locate and shut down illicit websites that sell medications; and (2) raise public knowledge of consumer rights. To discourage the establishment of illicit pharmacies, the draft rules must additionally contain a provision imposing accountability in the form of a fine or criminal prosecution.

According to the draft Rules, a prescription is a document from a licenced medical professional which can be written by hand or electronically made. Despite the fact that e-prescription is included in the Draft Rules, the policymakers have not fully addressed the matter. The new regulations emphasise that it is the duty of internet pharmacies to confirm the legitimacy of prescriptions. This method will not be totally successful, and customers should also be held accountable for providing fraudulent prescriptions or using the same prescription on many websites.

The regulation of lifestyle medications is another issue that the draft rules fail to acknowledge. There are now medications on the market that promise to help people lose weight, grow hair, cut back on their cravings for alcohol, cigarettes, and overeating, as well as improve their lifestyle. These medications, also known as "lifestyle drugs," are typically available without a prescription and do not fall under the category of controlled substances. Even if lifestyle medicines cannot cause addiction, they can still be harmful to those who already have other health problems, hence laws are required to guarantee the safe and secure distribution of these drugs.

Other issues include:

Data privacy: Everyone is entitled to privacy as a fundamental right. However, the regulations now in place say nothing about how these e-pharmacies would handle patient personal data that they will have access to. Data is the new gold in today's society; thus, the government must make sure that it is not exploited.

Mechanism of regulation: The State licencing authorities oversee the registration of pharmacies and the selling of pharmaceuticals. On the other hand, e-pharmacies can operate across India after registering at a certain location. Thus, the question is raised as to how different State regulators will handle these online pharmacies. As a result, guidelines for the commercial operations of online pharmacies must be developed including inter-state sales.

Anti-competitive behaviour: Through their association, the All-India Organisation of Chemists & Druggists (AIOCD) and other traditional pharmacies are demonstrating against e-pharmacies, claiming that they are operating illegally and engaging in anti-competitive behaviour by giving customers steep discounts, which completely goes against the principles of a free market.

## Present position of e-pharmacy regulation in India

Despite the fact that the Indian government has drafted new rules to change the D&C rules, they have not yet been notified in the official gazette and are awaiting implementation. In a number of petitions, the Hon. High Courts of Delhi and Madras requested that e-pharmacy activities be prohibited for the sake of the safety of the public. Both Honourable Courts supported outlawing the online sale of pharmaceuticals and medical supplies, and the Honourable High Court of Madras in *T.N. Chemists and Druggists Assn. v. Union of India* even went so far as to ask the government to enact new regulations governing the internet selling of medications. Furthermore, the Delhi High Court's December 2018 ruling in the *Zaheer Ahmed v. Union of India* case forbade the online sale of pharmaceuticals without a licence. The Drugs Controller General of India (DCGI) notified all drug controllers of this development in an official letter issued on November 28, 2019.

## CONCLUSION

It is evident that the market for online pharmacies has already firmly established itself in the online medicine sales industry. Based on the numbers and overall situation, it appears that e-pharmacies are moving past the experimental stage and are starting to take shape. An actual illustration of this is how helpful e-pharmacies were during COVID-19. Furthermore, the law must evolve along with technology whenever it advances. Another contention is that because the marketplace-based e-pharmacies lack a pharmacist with a valid licence, they are unable to display drugs on their websites because the law only permits licence holders to do so. However, the marketplace model e-pharmacies contend that, in accordance with the Information Technology Act of 2000, they are merely intermediaries, linking buyers and sellers through their websites. The issue concerning if they may show pharmaceuticals on their website then comes up. The government must remove these barriers by making minor changes to the pre-independence era legislation. Rather than considering outright prohibiting e-pharmacies, the government should create a solid plan and provide precise regulations to deal with some of the present problems, such as fraudulent prescriptions, sales between states, etc.

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Research Article

# TO ASSESS AWARENESS OF HEALTHCARE PROFESSIONALS AND STUDENTS TOWARDS PHARMACOVIGILANCE, MATERIOVIGILANCE, VACCINE SAFETY SURVEILLANCE AND NATIONAL POISON INFORMATION CENTRE IN GANGTOK, SIKKIM.

***Shailee Dewan**


## ABSTRACT

**Background:**
Surveillance plays a pivotal role in providing insight into a lacuna and help the system to address it. Pharmacovigilance, Materiovigilance, Vaccine safety surveillance and Toxicovigilance programmes were started with the aim to address the need for surveillance and intervention.

**Aim:** To assess questionnaire-based survey on awareness of healthcare professionals and students of Gangtok, Sikkim towards Pharmacovigilance programme of India, Materiovigilance programme of India, Vaccine Safety Surveillance and National Poisons Information Centre.

**Objective:**

1. To assess the level of awareness among different individuals from questionnaires.
2. To investigate the role of ADR for mitigating the country's economic burden and improving quality of life.
3. To generate meaningful insight from the integration of data for improving spontaneous reporting among healthcare professionals.

**Methodology:**
A cross sectional questionnaire-based awareness study was conducted among healthcare professionals and students. The survey was designed using the information from the literature to assess the awareness among the healthcare professionals and students indulged in patient care andvarious literature were reviewed to investigate the role of ADR for mitigating the country's economic burden and improving quality of life.

**Result:**
The survey was completed with 172 participants. Out of the 172 participants, 132 (76.7%) were aware of the term PvPI, 82 (47.7%) were aware of the term MvPI, 135(78.5%) were aware of the term Vaccine Safety Surveillance and only 67 (39.0%) were aware of the term NPIC.


**Key words:** Pharmacovigilance, Materiovigilance, Vaccine Safety Surveillance, National Poisons Information Centre.

## INTRODUCTION

Many unfortunate events in the past have led to the emergence of pharmacovigilance and the need as such arises for the same to reduce the morbidity and the mortality due to the adverse drug reactions and any drug related issues.

The origins can be traced back to more than 170 years ago on 28 January 1848, with the death of a 15-year-old Hannah Greener of Winlaton after receiving a chloroform anaesthetic for the removal of a toenail [1]. After this incident there has been many unfortunate tragedies that has led to pharmacovigilance [2] [3]. The incidence of ADRs may be even greater because some ADRs mimic natural disease states and may thus go undetected or unreported but are known to cause death in as many as 0.1%–0.3% of hospitalized patients [4].
Under the auspices of the Ministry of Health and Family Welfare, the Central Drugs Standard Control

Organisation (CDSCO), New Delhi, launched a nation-wide pharmacovigilance programme in July 2010, with the All-India Institute of Medical Sciences (AIIMS), New Delhi serving as the National Coordinating Centre (NCC) for monitoring Adverse Drug Reactions (ADR) in the country to protect public health. This Programme established 22 ADR monitoring centres (AMCs), including AIIMS in New Delhi, in 2010. In April 2011, the National Coordinating Centre was moved from the All-India Institute of Medical Sciences (AIIMS) in New Delhi to the Indian Pharmacopoeia Commission (IPC) in Ghaziabad, Uttar Pradesh to ensure more effective programme implementation which now functions as the National Coordination Centre (NCC)for the Pharmacovigilance Programme of India (PvPI) that focuses on promoting safer drug therapy to protect public health. India contributes about 3% to the global database in the form of PvPI[5][6]. These AMCs report ADRs to the National Coordination Centre (NCC) using VigiFlow, a software developed by WHO-UMC (Sweden)[5].

The expanded patient safety scope of pharmacovigilance covers the detection of low-quality drugs as well as prescribing, dispensing, and administration errors. Other pharmacovigilance concernsinclude counterfeiting, antibiotic resistance, and the requirement for real-time surveillance in bulk vaccinations [6].

The poison information centre has grown globally with the need to reduce the morbidity and mortality due to poisoning especially in a developing country with high-rate industrialization and urbanization rate [7][14]

## AIM AND OBJECTIVES

2.1. ***Aim:*** To assess questionnaire-based survey on awareness of healthcare professionals and students towards Pharmacovigilance programme of India, Materiovigilance programme of India, Vaccine Safety Surveillance and National Poisons Information Centre.

*2.2.* ***Objective:***

2.2.1. To assess the level of awareness among different individuals from questionnaires.

2.2.2. To investigate the role of ADR for mitigating the country's economic burden and improving quality of life.

2.2.3. To generate meaningful insight from the integration of data for improving spontaneous reporting among professionals.

## METHODOLOGY

*Survey Design and Data Collection*: A cross-sectional study was conducted among healthcare professionals and students to assess their awareness towards Pharmacovigilance programme of India, Materiovigilance programme of India, Vaccine Safety Surveillance and National poison Information Centre.

*Survey Sample*: The study included healthcare professionals and students from different institutions mainly focused in Gangtok, Sikkim.

*Survey Questionnaire*: The survey was distributed in English and involves 5 sections which includes sociodemographic data,awareness towards Pharmacovigilance Programme of India (PvPI), awareness towards Materiovigilance Programme of India (MvPI),awareness towards vaccine safety surveillance and awareness towards National Poison Information Centre.

*Sample Analysis*: The data were collected initially using Microsoft excel, furthered cleaned and coded using IBM SPSS Statistics version 29.0.1.0. Multi response was tabulated for dichotomy group valued at 1.

## RESULT

***Sociodemographic results***

The sociodemographic data of the participants (Table 1.) indicated, out of 172 participants, (n=47 male,27.3%), (n= 124, 72.1%) and (n=1 others,0.6%) with age ranging 20or below(n=19,11.0%), 21-30(n=130,75.6%), 31-40(n=16,9.3%), 41-50(n=4,2.3%), 51-60(n=3,1.7%) were involved. From the total participants 61 were from GPC, 48 from SMIMS, 6 from SGCN, 7 from SPU, 16 from STNM, 10 from CRH, 15 from HPI and 9 from other institutions all over in Sikkim. Furthermore, about (n=82, 47.67%) of the participants were from Bachelor in Pharmacy background (n=57, 33.14%) were from BSc. Nursing background, (n=15, 8.72%) were from MBBS background and (n=18, 10.47) were from other degrees that indulge in healthcare, the detailed response is mentioned in figure 1. Out of 172 participants students were (n=133, 77.3%) and professionals were (n=39, 22.9%).

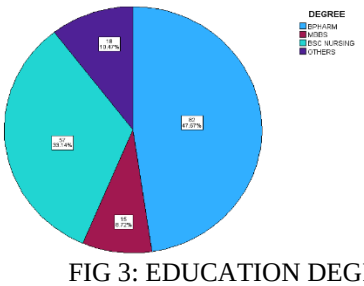


FIG 3: EDUCATION DEGREE

| *Table no.1 Sociodemographic data* Variable | | Count | Table N % |
|---|---|---|---|
| INSTITUTION NAME | GPC | 61 | 35.5% |
| | SMIMS | 48 | 27.9% |
| | SGCN | 6 | 3.5% |
| | SPU | 7 | 4.1% |
| | STNM | 16 | 9.3% |
| | CRH | 10 | 5.8% |
| | HPI | 15 | 8.7% |
| | OTHERS | 9 | 5.2% |
| AGE | 20 OR BELOW | 19 | 11.0% |
| | 21-30 | 130 | 75.6% |
| | 31-40 | 16 | 9.3% |
| | 41-50 | 4 | 2.3% |
| | 51-60 | 3 | 1.7% |
| | 61-70 | 0 | 0.0% |
| GENDER | FEMALE | 124 | 72.1% |
| | MALE | 47 | 27.3% |
| | OTHERS | 1 | 0.6% |
| CATEGORY | STUDENT | 133 | 77.3% |
| | PROFESSIONAL | 39 | 22.7% |

| *Table 2.* Dichotomy group tabulated at value 1. | | | |
|---|---|---|---|
| *Questionnaire* | | Correct Response N | Percent of response |
| Variables | 1.WOULD YOU HAPPEN TO BE AWARE OF THE CONCEPT OF PHARMACOVIGILANCE PROGRAMME OF INDIA? | 132 | 76.7% |
| | 2.WOULD YOU HAPPEN TO BE AWARE OF THE HEALTH AND FAMILY WELFARE, GOVERNMENT OF SIKKIM INITIATIVE IN PHARMACOVIGILANCE PROGRAMME OF INDIA? | 112 | 65.1% |
| | 3.PHARMACOVIGILANCE IS RELATED TO | 140 | 81.4% |
| | 4.PHARMACOVIGILANCE DETECTS | 102 | 59.3% |
| | 5.PHARMACOVIGILANCE CENTRE IN SIKKIM IS PRESENT AT | 86 | 50.0% |
| | 6.IN YOUR EXPERIENCE, WHICH HEALTHCARE PROFESSIONAL IS TYPICALLY RESPONSIBLE FOR REPORTING AN ADVERSE DRUG REACTION(ADR)? | 101 | 58.7% |
| | 7.PHARMACOVIGILANCE PROGRAMME OF INDIA IS OVERSEEN BY | 69 | 40.1% |

| | | | |
|---|---|---|---|
| | 8.IN YOUR OPINION WHAT WOULD YOU SUGGEST: 'REPORTING OF ADVERSE DRUG REACTION IS' | 161 | 93.6% |
| | 9.WOULD YOU RECEIVE ANY ELECTRONIC UPDATE RELATED TO PHARMACOVIGILANCE PROGRAMME? | 91 | 52.9% |
| | 10.WOULD YOU HAPPEN TO BE AWARE OF THE MATERIOVIGILANCE PROGRAMME OF INDIA? | 82 | 47.7% |
| | 11.WOULD YOU HAPPEN TO BE AWARE OF THE HEALTH AND FAMILY WELFARE, GOVERNMENT OF SIKKIM INITIATIVE IN MATERIOVIGILANCE PROGRAMME? | 75 | 43.6% |
| | 12.ARE YOU AWARE OF THE PROCESS FOR REPORTING ADVERSE EVENTS ASSOCIATED WITH MEDICAL DEVICES TO THE MATERIOVIGILANCE PROGRAMME OF INDIA? | 80 | 46.5% |
| | 13.MATERIOVIGILANCE IS RELATED TO | 102 | 59.3% |
| | 14.MATERIOVIGILANCE PROGRAMME OF INDIA IS OVERSEEN BY | 68 | 39.5% |
| | 15.WERE YOU AWARE THAT GOVERNMENT PHARMACY COLLEGE, SAJONG IS A MEDICAL DEVICES ADVERSE EVENT MONITORING CENTRE? | 78 | 45.3% |
| | 16.WOULD YOU RECEIVE ANY ELECTRONIC UPDATE RELATED TO MATERIOVIGILANCE PROGRAMME? | 74 | 43.0% |
| | 17.WOULD YOU HAPPEN TO BE AWARE OF THE VACCINE SAFETY SURVEILLANCE? | 135 | 78.5% |
| | 18.VACCINE SAFETY SURVEILLANCE IS RELATED TO | 84 | 48.8% |
| | 19.ARE YOU AWARE OF THE REPORTING PROCESS FOR ADVERSE EVENT FOLLOWING IMMUNIZATION? | 93 | 54.1% |
| | 20.WOULD YOU HAPPEN TO BE AWARE WHICH BODY IS RESPONSIBLE FOR OVERSEEING ADVERSE EVENT FOLLOWING IMMUNIZATION? | 61 | 35.5% |
| | 21.WOULD YOU HAPPEN TO USE/REPORT AN AEFI FORM? | 45 | 26.2% |
| | 22.WOULD YOU RECEIVE ANY ELECTRONIC UPDATE RELATED TO VACCINE SAFETY SURVEILLANCE? | 61 | 35.5% |
| | 23.WOULD YOU HAPPEN TO BE AWARE OF THE NATIONAL POISON INFORMATION CENTRE? | 67 | 39.0% |
| | 24.NATIONAL POISON INFORMATION CENTRE PROVIDES INFORMATION RELATED TO | 120 | 69.8% |

| | | | |
|---|---|---|---|
| | 25.WOULD YOU HAPPEN TO EVER CONTACT OR SOUGHT GUIDANCE FROM THE NATIONAL POISON INFORMATION CENTRE REGARDING POISON-RELATED CASES OR INQUIRIES? | 34 | 19.8% |
| | 26.NATIONAL POISON INFORMATION CENTRE IS BASED AT | 95 | 55.2% |
| | 27.ARE YOU FAMILAR WITH THE HOTLINE NUMBER OR CONTACT INFORMATION OF THE NATIONAL POISON INFORMATION CENTRE FOR IMMEDIATE POISON-RELATED EMERGENCIES OR CONSULTATIONS? | 31 | 18.0% |

Table 2 indicates the dichotomy group tabulated at value 1. For the question regarding the awareness towards PvPI (n=132, 76.7%) and regarding the H&FW department initiative (n=112,65.1%) responded positively. (n=140, 81.4%) gave correct response to 'pharmacovigilance is related?' to and (n=102, 59.3%) gave correct response to 'pharmacovigilance detects?'. (n=101, 58.7%) showed positive response that all healthcare professionals are responsible for reporting and (n=161, 93.6%) considered that reporting is necessary. (n=69, 40.1%) responded that IPC oversees the PvPI and (n=91, 52.9%) responded positively towards 'receiving electronic update related to PvPI? (n=82, 47.7%) responded positively that they were aware of the MvPI, (n=75, 43.6%) responded yes to 'aware of the initiative of H&FW department, Sikkim towards MvPI. (n=80, 46.5%) were aware of the process for reporting adverse events related to the medical devices. (n=68, 39.5%) responded that IPC oversees MvPI. (n=78,45.3%) were aware that Government Pharmacy College, Sajong is a medical device Adverse event monitoring centre. Only (n=74, 43.0%) responded positively to 'receiving to electronic update to MvPI?'(n=135,78.5%) were aware of the Vaccine safety surveillance. Only (n=84, 48.8%) responded correctly to 'vaccine safety surveillance is related to?'. (n=93,54.1%) were aware of the process for reporting an AEFI and (n=61,35.5%) were aware of the body responsible for overseeing AEFI. (n=61, 35.5%) responded yes to 'use/report an AEFI form?' and (n=61,35.5%) responded yes to 'receiving any electronic update to vaccine safety surveillance'. (n=67, 39.0%) were aware of the NPIC and (n=120,69.8%) responded correct to' NPIC provides information related to?'. (n=34, 19.8%) have sought guidance from the NPIC. (n=95,55.2%) were aware where the NPIC was based at and (n=31, 18.0%) were aware of the hotline number of the NPIC.

## DISCUSSION

This study observed that the respondents was least aware of the National Poison Information Centre (39%) followed by Materiovigilance programme of India (47.7%), Pharmacovigilance programme of India (76.7%) and then the Vaccine safety surveillance (78.5%). Only (26.2%) had use/reported using an AEFI form even though the respondents were aware of the Vaccine safety surveillance (78.5%) which implies reporting culture is still lacking. Majority (93.6%) of the respondents considered reporting as necessary but approximately, only half of the majority were aware of the reporting process.

To overcome these concerns and to improve the spontaneous reporting system among healthcare professionals we can suggest:

1. Opening job vacancies for clinical pharmacist in hospitals for clinical integration of pharmacist in general practice.
2. Awareness is key to improve spontaneous reporting and awareness among general public is as necessary as in healthcare professionals.
3. Providing financial incentives, training courses, improvement of the computer system and regular publishing of the ADR information are also some of the few interventions that aid in improving spontaneous reporting.
4. Establishment of pharmacovigilance system in hospital and ensuring availability of ADR reporting forms.
5. Alerting the physician about the list of ADR to be reported and practice stimulated reporting.
6. KAP studies among healthcare professionals to provide insight about the status of their knowledge, attitude and practice towards reporting and taking appropriate interventions. [26,27,28]

Efforts to improve spontaneous reporting and addressing adverse drug reaction will not only mitigate country's economic burden but will also contribute to improving the quality of life and public health.

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Review Article

# A Systematic short review on *Clitoria ternatea*: Pharmacological activities and Phytochemicals

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## ABSTRACT

*Clitoria ternatea* is perennial herbaceous plant from family Fabaceae. It has potential applications in modern medicine as well as agriculture. Ita is also used as natural food colorants and antioxidant. The present review contains the information related to Clitora ternatea phytochemicals and its pharmacological activity. This paper reviews plant distribution, phtyconstituents like - flavonaols-kaempferol, kaempferol 3-glucoside, kaempferol 3-robinobioside-7-rhamnoside, Quercetin, anthocyanins, etc. It also includes the different pharmacological acivities were shown by Clitoria ternatea like anti-inflamatory, antioxidant, catheratics, insecticides etc.

**Keywords**: *Clitoria ternatea*, pharmacological activity, phytoconstituents, antidiabetic, antioxidant

## INTRODUCTION

Plant and herbs have play important rolein human life for thousands of years. Most of them are well known medicinal herbs [1]. Butterfly pea or blue pea (clitoria ternatea) is from family fabaceae and sub-family papilionaceae[2].It is perennial herbaceous plant, which originated from tropical region of India ,Sri Lanka, Malaysia, Burma, and Philippine islands[3,4]. Clitoria ternatea flower are commercially known as Bungatelang by the locals and are Widely used as the food dyes in Nasikerabu (It is an the local dish in Kelantan, Malaysia) and a Baba and Nyonya kueh known as kuehtekan[1]. The newly obtained C. ternatea anthocyanins termed “ternatins” which render C. ternatea flowers with their vivid blue color, were first isolated in 1985[8,17]. Study of flowers suggested that it having health beneficial properties, such as tranquilizing effect, anti-inflamatory and antipyretic activities [7,15]. The difference parts extract of Clitoria ternatea had different efficacy against the tested microorganisms. These obtained differences could be due to the nature and level of the antimicrobial agents present in the extracts and their mode of action on the different test microorganisms [1,16]. This plant have been used in Sri Lankan traditional system of medicine and in folklore ton treat variety of disorders such as anasarca, ascites, liver problems, hemicrania, irritarion of urethra and bladder, and enlargement of abdominal viscera [9].Clitoria ternatea flower is a source of natural blue food and beverage colorant worldwide[10]. Butterfly pea is one of the major sources of natural color used in food and cosmetics. Anthocyanins are present in its petals which is main coloring constituent and could be extracted easily with water. We found that the ph of medium, temperature, and light affect stability of the color aqueous extract from butterfly pea petals.[13]. Due to their high reactivity, non-hazardous and better efficiency are reason behind their wider applications than the human-made compounds, the natural compounds have many interdisciplinary applications also[3]. Evaluation of chemical diversity among genotype of medicinal plants plays a crucial role in improvement and large-scale cultivation. Chemical variability of bioactive principles viz. taraxerol and beta-sitosterol are analyzed in 11 populations of clitoria ternatea L., it is an important memory enhancer used in Ayurveda [14].

## COMMON NAME

Bengali:Aparajita,
English:Butterfly pea , blue pea vine , mussel- shell climber, pigeon wings, Sanskrit: Sankhapushpi , aparajita, saukarnika, adrakarni , girikarnikasupuspi , mohansini , vishadoshaghani , shwetanama , vishnukranta , Kannada ashwakhura ,
Hindi:Koyala ,
Telgu: Dintena,
Malyalam: sangupushpam: Nagar hedi,
Mrathi: Gokarna,
Portuguese: Fulacriqua,

**Synonyms**
Clitoriaalbiflora Mattei
ClitoriabracteatePoir.
Clitoria coelestrissieberts and Voss
Clitoria parviflora Raf.
Clitoria phillippensis Per.
Clitoria pilosulaBenth.
Clitoria ternatensium Crantz
Ternatea vulgaris Kunth
Ternatae vulgaris Kuntze

## PHYTOCHEMICALS

### A. Flavonols

*Clitoria ternatea* seeds contain flavonol glycosides as well as phenolic aglycones, cinnamic acid, and a range of other compounds . there are different flavonols were present in C. ternateaflavonols, namely kaempferol, kaempferol 3-glucoside, kaempferol 3-robinobioside-7-rhamnoside, quercetin, and quercetin 3-glucoside Subsequent studies reported the isolation of flavonol glycoside from C. ternatea leaves and flowers [15-17].
Following are some flavones with their structure.

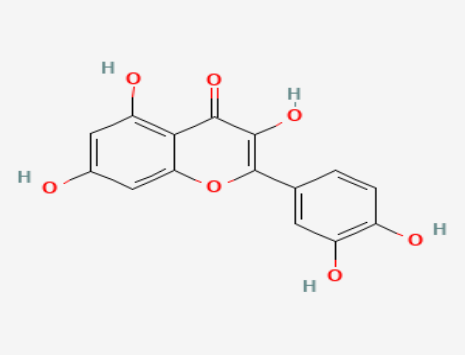

**Fig. No. 1: Structure of Quercetin**

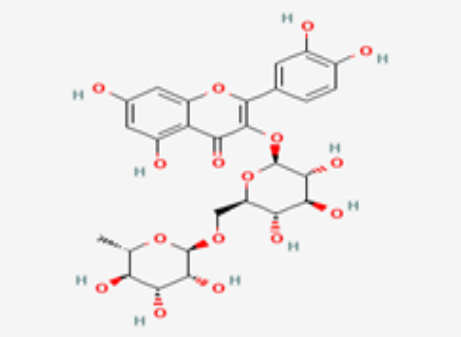

**Fig. No. 2: Structure of Quercetin3-rutinoside**

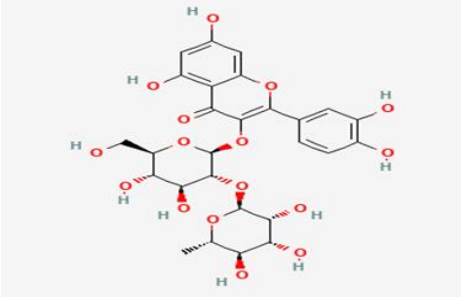

**Fig. No. 3: Structure of Quercetin 3-neohesperidoside**

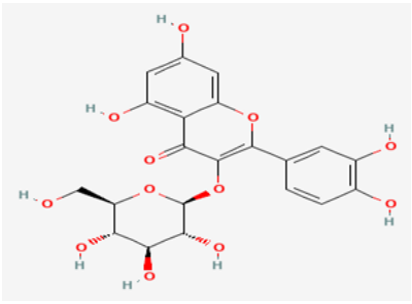

**Fig. No. 4: Structure of Quercetin 3-glucoside**

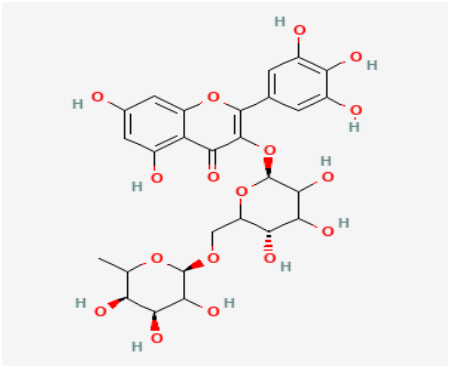

**Fig. No. 5: Structure of Myricetin 3-rutinoside**

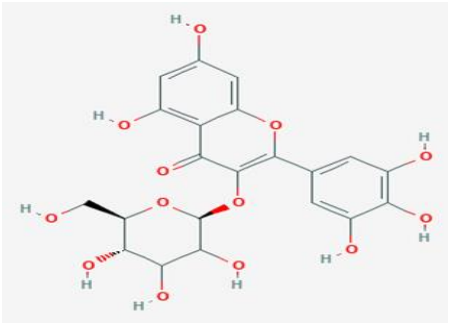

**Fig. No. 6: Structure of Myricetin 3-glucoside**

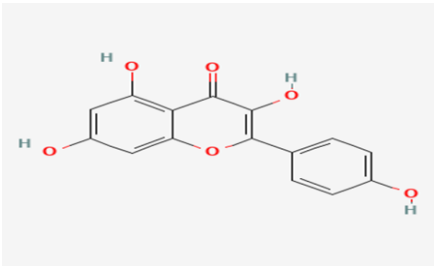

**Fig. No. 8: Structure of Kaempferol**

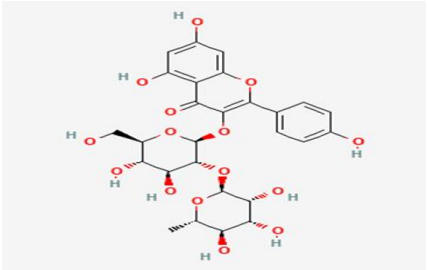

**Fig. No. 9: Structure of Kaempferol 3-neohesperidoside**

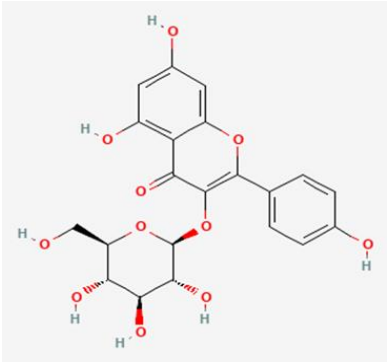

**Fig. No. 10: Structure of Kaempferol 3-glucoside**

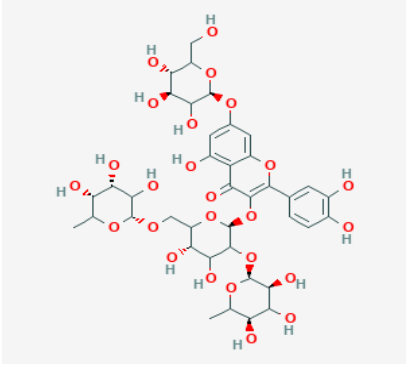

**Fig. No. 11: Structure of Quercetin 3-(2g-rhamnosylrutinoside)**

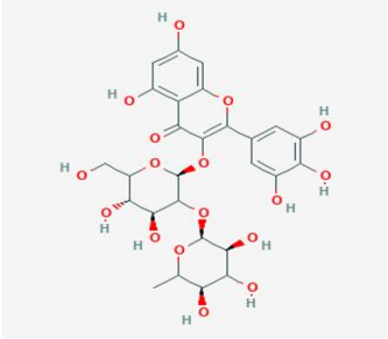

**Fig. No. 12: Structure of Myricetin 3-neohesperidoside**

## ANTHOCYANINS

Six acylated anthocyanins were isolated from blue C. ternatea flowers that were all derivatives of delphinidin 3,3',5'-triglucoside, The chemical properties of the acylated C. ternateadelphinidins, which were named ternatins, were further elucidated in subsequent studies. The structure of the largest isolated blue anthocyanin, ternatin A1, was determined 18]. The study also showed that not only was ternatin A1 the largest, it was one of the most stable in neutral solution The structure of ternatins A2B1 B2[19] were elucidated shortly after. Subsequent studies isolated and determined the structures of several other novel ternatins isolated from C. ternatea: ternatins A3, B3-B4,C1-C5,D3, and preternatins A3 andC4 [19].

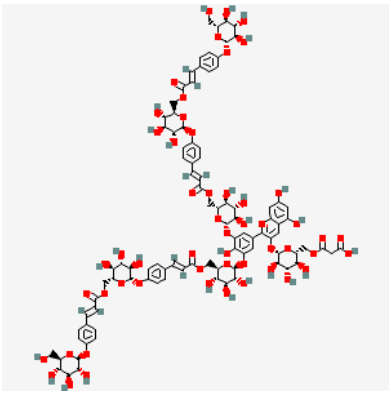

**Fig. No. 13: Structure of Ternatin A1**

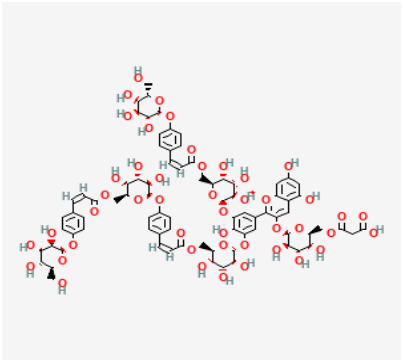

**Fig. No. 14: Structure of Ternatin A2**

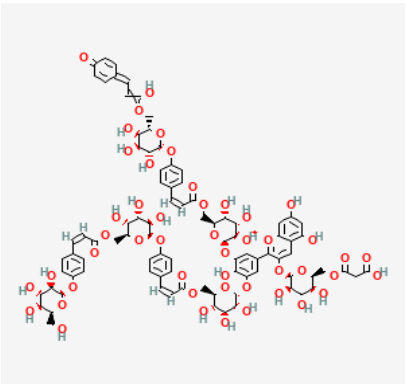

**Fig. No. 15: Structure of Ternatin B1**

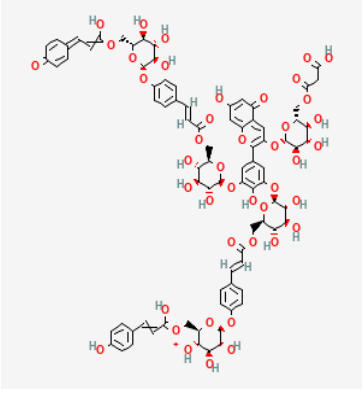

**Fig. No. 16: Structure of Ternatin D1**

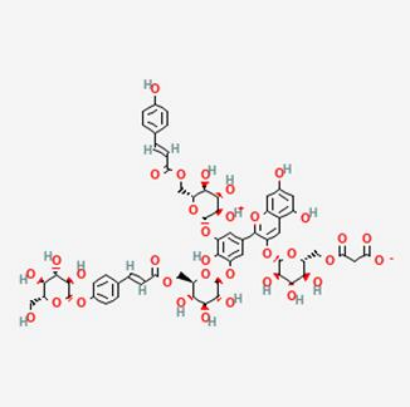

**Fig. No. 17: Structure of Ternatin B4**

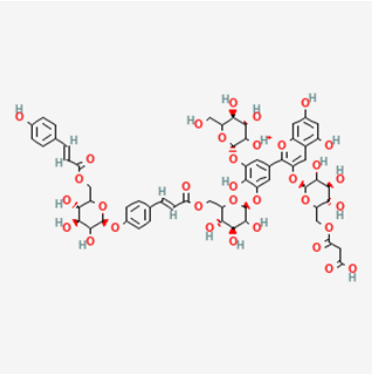

**Fig. No. 18: Structure of Ternatin C1**

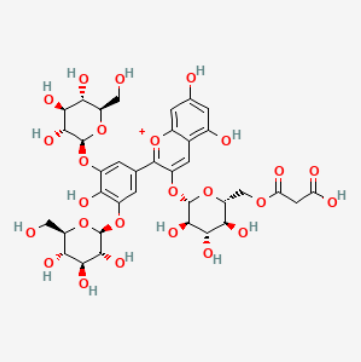

**Fig. No. 19: Structure of Ternatin C5**

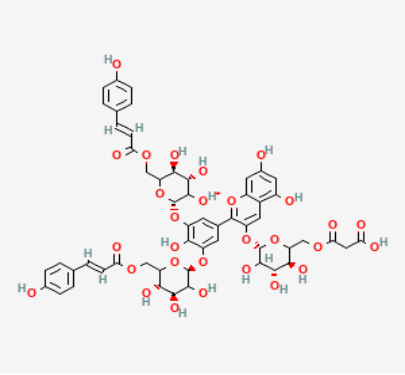

**Fig. No. 20: Structure of Ternatin D3**

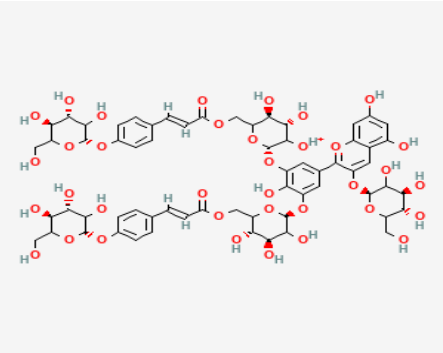

**Fig. No. 21: Structure of Preternatin A3**

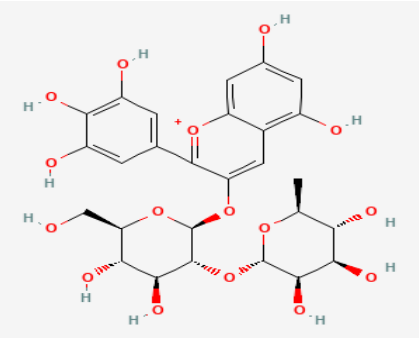

**Fig. No. 22: Structure of Delphinidine 3-neohesperidoside**

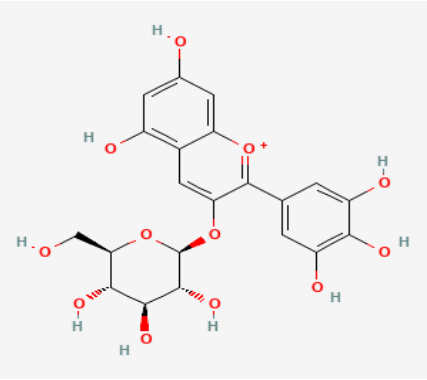

**Fig. No. 23: Structure of Delphinidine 3-glucoside**

## Other Non-proteinaceous Components

The pentacyclic triterpenoids, taraxerol and taraxerone, were isolated from roots of C. ternatea .C. ternatea as a source of taraxerol Its roots also contains taraxerol, novel norneolignans, clitorienolactones A-C,. C. ternateafloral extracts also contain other types of flavonoids, including rutin (flavone), epicatechin (flavanol) and other polyphenolic acids (gallic acid, protocatechuic acid, and chlorogenic acid) [19, 20]

**Table No. I: Table showing different parts of *C. ternatea* plant with its phytochemicals and function**

| Plant Parts | Phytochemicals | Functions | References |
|---|---|---|---|
| Leaf | Alkoloids, Reducing suger, Flavonoids, Steroids, Glycosides | 1. Prevention of neurodegenerative diseases and diabetes mellitus 2. Effectively controls the excessive sweating | [21] |
| Flower | Saphonin, Tanin, Alkoloids, Glycosides, Phytosterols, Carbohydrates | 1.Anti-inflammatory, Analgesic 2.Ethanol extract is used as antidiabetic | [22,23] |
| Root | 1,1-Diphenyl-2-picrylhydrazyl(DPPH) | 1.Antioxidant 2.diuretic and laxative | [24] |
| Seed | The seeds contain nucleoprotein with its amino-acid sequence similar to insuline , delphinidin-3,3,5-triglucoside, essential amino acids, anthosxanthin glucosides, 3,5,7,4-tetrahydroxy-flavone-3-rhamoglycoside,p-hydroxy cinnamic acid polypeptide, | 1.cathartic purgative and aperients | [25] |

## Pharmacological Activities

### 1. Anxiolytic activities

Oral treatment with alcohol extract of clitoria ternatea at a dose of 460 mg/kg significantly prolonged the time taken to traverse the maze as produced by chlorpromazine in rat demonstrated significant effect on anxiety. The animal treated with clitoria ternatea (100 mg/kg) showed a significant increase in the inflexion ratio and discrimination index which provides evidence for the species nootropic activity [1]

### 2. Anti-epileptic activity studies

Methanol extract from the aerial parts of clitoria ternatea screend by using pentylenetetrazol (PTZ) and maximum electroshock (MES)- induced seizures in mice at the dose of 100 mg/kg p.o. CT significantly delayed the onset of convulsions and also delayed the duration of tonic hind limb extension in MES- induced convulsions [2]

### 3. Antimicrobial Activity

Different extracts of Clitoria ternatea showed inhibitory effects against Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumonia, Bacillus subtilis, AeromonasFormicans, Aeromonashydrophila and Streptococcus agalactiae. Ethyl acetate extracts of Clitoriaternatea showed maximum zone of inhibition against A. Formicans , A. hydrophilia B. subtilis and P. aeruginosa next to that ethanol extract of Clitoria ternatea showed maximum zone of inhibition against A. formicans and E. coli followed by the acetone extract which showed maximum zone of inhibition against S. agalactiae and K. pneumonia . [12]

### 4. Anticancer effect

The in vitro cytotoxic effect of petroleum ether and ethanolic flower extracts (10, 50, 100, 200, 500 µg/ml) of Clitoria ternatea was studied using trypan blue dye exclusion method. Both extracts exhibited significant dose dependent cell cytotoxic activity. For petroleum ether extract the concentration 10 µg/ml showed 8% reduction in cell count, however, 100% reduction was observed at 500 µg/ml. In case of ethanolic extract, 10 µg/ml concentration possessed 1.33% reduction in cell count, while, at 500 µg/ml 80% reduction in cell count was observed. [24]

### 5. Wound healing effect

The wound healing activity of Clitoria ternatea seed and root extracts was investigated using excision, incision and dead-space models in rats. Clitoria terntea seed and root extracts significantly improved wound healing in excision, incision and dead-space models when administered orally by gavages as well as applied topically as ointment. These effects were comparable to that of cotrimoxazole ointment. The finding of the study also showed that Clitoria ternatea affected all three

phases: inflammatory, proliferative and remodeling phases of wound healing. [23]

## 6. Gastrointestinal effect

The antiulcer potential of aqueous and ethanolic extracts of Clitoria ternatea was evaluated was evaluated in differed in different experimentally induced ulcer models in rats. Ethanolic extract (200 and 400 mg/kg) and aqueous extract (200 and 400 mg/kg) of whole plant were examined in pylorus ligation and indomethacin induced gastrc ulcer in rats. Various parameters like volume of gastric acid secretion, pH, total acidity, ulcer index and antioxidant parameters were determined and compared between extracts, standard and vehicle control group following ulcer induction. Among different dose of alcoholic extract, high dose showed significant antiulcer activity in pylorus ligation and indomethacin induced ulceration [20].

## 7. Insecticidal Activity

Proteins and peptides isolated from C. ternatea are reported to exhibit insecticidal properties (Kelemu et al., 2004; Poth et al., 2011a) (Table 5). One study reported 100% larval mortality when 1% w/w of the purified C. ternatea protein (20 kDa), finotin, was applied to the bruchidsAcanthoscelidesobtectus and Zabrotessubfasciatus, respectively (Kelemu et al., 2004). Another study showed that when the lepidopteran species Helicoverpaarmigera, larval growth retardation was observed in a dose dependent at 1µmol CterM peptide g-1 diet. [23]

## 8. Anthelminthic Activity

The methanolic extract of C. ternatea was also found to inhibit 93% of M. incognita egg from hatching. In another study that utilized the model organism, Caenorhabditis elegans, C. ternatea extracts were found to effectively kill nematode larvae, with the root extracts showing greater lethality than the leaf extracts [26].

## 9. Anti-diabetic studies

Oral administration of aqueous extract of CT leaves (400mg/kg body weight) and flowers (400mg/kg body weight) for 84 days showed significantly reduced serum glucose, glycosylated hemoglobin, total cholesterol, triglycerides, urea, creatinine and the activity of gluconeogenic enzyme glucose-6-phosphatase, but increased serum insulin, HDL-cholesterol, protein, liver and skeletal muscle glycogen content and the activity of glycolyt7ic enzyme glucokinase. For all the above biochemical parameters investigated, Clitoriaternatea leaves treated rat showed a little better activity than Clitoria ternatea flowers treated diabetic rats.[22]

## CONCLUSION

*Clitoria ternatea* is perennial herbaceous plant from family Fabaceae. It has potential applications in modern medicine as well as agriculture.C. ternatae is garden plant of India, which has been used in traditional as well as mordern medicines nowadays. This review paper includes plant distribution, phtyconstituents like- flavonaols- kaempferol, kaempferol 3-glucoside, kaempferol 3-robinobioside-7-rhamnoside, Quercetin, anthocyanins, etc. It also includes the different pharmacological acivities were shown by Clitoria ternatea like anti-inflamatory, antioxidant, catheratics, insecticides etc. From this study it conclude that C. ternatea is a very effective plant whiuch will be benifical for future drug development form natural origin.

## Acknowledgements

We would like to thank Dr. R. S. Adnaik, Anandi Pharmacy College, Kalambe tarf Kale, Kolhapur for providing the necessary laboratory facilities.

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Research Article

# DESIGN, DEVELOPMENT OF PROBIOTIC GUMMIES AND DETERMINING THE STABILITY OF GUMMIES

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**ABSTRACT:**

Probiotics have been said to assist healthy immunological and digestive systems. *B.coagulans* has become a focus of research due to its high temperature stable, highly viable, economical and Versatile in nature. The ultimate objective of the present research work is to incorporate *B.coagulans* strain into the gummies, which will benefit the human health. Gummies are formulated by Trio method. Optimization studies for ingredients was carried out to determine the concentration which is ideal for the preparation. Two different formulations were prepared with the help of Optimization data using sucrose, gelatin and pectin as the base for the preparation of gummies. All the prepared probiotic gummies were subjected to various evaluation parameters like pre-formulation studies, microbial analysis, nutritional facts and Stability data. The results of microbial analysis shows that viability of probiotic in gummy is not less than 500 million spores /gummy, total yeast and mold count is < 10 Cfu /gummy and Pathogen are absent in the formulations. Nutritional facts determines the content like Carbohydrate and Total Sugar content varied from 75.1% to 82.76% w/w and 65.4% to 79.91% w/w. Fat and protein in gummies with *B.coagulans* varied from 0.03 % to 0.78 % and 9.9 % to < 1%, respectively. The energy value of gummies varied from 338 kcal/100 g to 340 kcal/100gm. Short-term stability Studies indicate that there are no significant changes in physical characteristics, viable count, traces of yeast & mold and pathogens after 180 days of storage at 25±2º C with 60±5% RH.

**Key words:** *B.coagulans*, Viability, Nutritional facts, Stability studies

## INTRODUCTION

Probiotics are live microorganisms that are meant to improve one's health whether taken orally or topically. They can be discovered in yoghurt and other fermented foods, nutritional supplements and cosmetics. Numerous bacteria could be present in probiotics. The most prevalent bacteria come from the families *Lactobacillus, Bifidobacterium and Weizmannia coagulans.* Yeasts like, *Saccharomyces boulardii* and other microorganisms can both be employed as probiotics [1].

Probiotics helps in Optimal digestion, Vitamin Production, Supports Immunity, Decrease Cholesterol level and weight loss therapy [2]. *Bacillus coagulans (Weizmannia coagulans)* was initially discovered and reported in 1915 by B.W. Hammer at the Iowa Agricultural Experiment Station as the root of a coagulation epidemic in evaporated milk packaged by an Iowa condensary. . *Bacillus coagulans* is a spore-forming, motile, gram-positive, and catalase-positive and measures roughly 0.9 µm by 3.0 µm to 5.0 µm When the growth cycle enters the stagnant phase, it could appear Gram negative. The range of temperatures permitted is 30-55 °C (86-131 °F), with 50 °C (122 °F) being the ideal temperature for growth. [3]. *Bacillus coagulans* or *Lactobacillus sporogeneses* is a kind of probiotic bacteria and it has tolerance to high temperatures. Because of this, it does not require refrigeration and is shelf-stable. *B.coagulans* balance the micro-organism in the gut, controls the blood pressure, relieves depression, anxiety, insomnia and improves sleeping pattern. [4]

Manufacturers consider *B.coagulans* because it is economical, highly temperature stable, never arrive dead, and versatile in nature. Traditional supplements are ones that are swallowed whole in the form of a capsule or tablets. Probiotic Gummies can be chewed rather than consumed whole. Most of gummies taste good, which makes it simpler to remember to take them every day. Gummy supplements are manufactured using substances like gelatin, corn syrup, pectin fiber, sugar, flavors and coloring in addition to probiotics. Probiotic gummies provide the same overall health advantages as probiotic capsules, primarily support for digestive health, immune system function and Gut health. Advantages of Gummies when

compared with Tablets and Capsule is serving size is small, taste better, safeguard is better and the pace of work is efficient. [5]

## RESEARCH INTENTION

The World Health Organization defines probiotics as "live bacteria that, when administered in sufficient proportions, impart a health benefit on the host." Many people in India have bad dietary habits, which have a variety of negative repercussions on our bodies. In India, the majority of people eat tainted food, which disturbs the body's digestive system. Invasive infections are a significant cause of increased morbidity and mortality in this population. [6] *B.coagulans* as probiotic in humans and animals has a long history and is well documented. Because *B.coagulans* can form spores, it can withstand high temperatures and the harsh conditions of the human stomach, which allows it to provide probiotic advantage Due to this Probiotic strains like *Bacillus coagulans* has nutritional value, research from all over the world has been focused on developing methods and products that treat irritable bowel syndrome, boost immunity, and aid in digesting. [7]

By 2023, it is anticipated that the probiotic market would grow to 15 USD billion. A market study revealed that probiotic supplements took advantage of emerging trends to promote probiotics [8]. The market for dietary supplements is anticipated to experience the greatest CAGR of 15.0% between 2015 and 2021. During the review period, the Asia - Pacific region is anticipated to have the quickest market growth. The rising consumer demand for probiotic components in food is what fuels this increase [9]. In terms of *B. coagulans* stability throughout the preparation and storage of functional foods, there is a dearth of scientific evidence. Determining *B. coagulans* survivability during the production process and storage conditions of functional food in the form of gummies is therefore necessary [10]. *Bacillus coagulans* has often been used in adults in doses of 1 – 2 billion (Cfu's) by oral route daily for 4 – 12 weeks [11]. The study goal was to ascertain how *B. coagulans* viability would be affected by the manufacture and storing processes for probiotic gummy preserves.

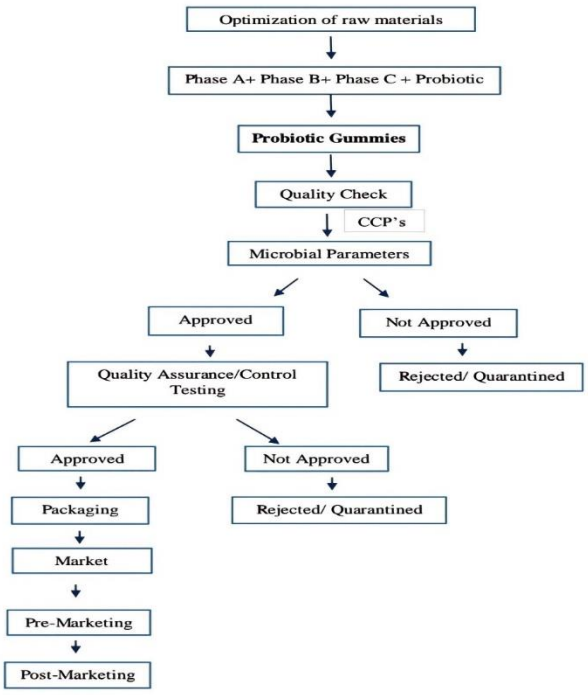



**Fig.1**. Work Plan for Design & Development of Probiotic Gummies

## MATERIALS AND METHODS

*Bacillus coagulans* samples used in the study were manufactured by Unique Biotech (Bangalore, India) Pure *B. coagulans* spores were spray–dried and standardized with food grade maltodextrin to achieve the desired concentration. Optimization Studies of Ingredient's were carried out to determine the Firmness, Strength and Hardness required to design the probiotic gummies. Two different formulations were designed using different gelling agents like Gelatin (Baker's Colors & Flavors) and Pectin (Maple Biotech Pvt.Ltd. Pune) were used as gelling agents, which give the soft texture to the gummies for the formulation (F1 & F2). B. *coagulans*, a probiotic, is incorporated into gummies. (100 billion Cfu/g), wherein Sucrose (Madhur Sugar, Shree Renuka Sugar Limited, Mumbai)contributes 40% of the weight of the gummies, Corn Syrup ( Karo, Light Corn Syrup Superme Traders, Mumbai), acts as a humectant and gives sweetness to the gummies, Citric Acid ( Blue Bird Food India Pvt.Ltd, Mumbai) acts as a preservative; and Flavoring & Coloring Agent (Bush, International Flavors & Fragrance India Pvt.Ltd, Chennai) give the gummies an attractive look and a pleasant taste while consuming them. Each Probiotic gummy weighs about 2.0g ±0.25g and contains NLT 500 million spores/gummy. Physical & Chemical Parameters of Gummies were determined. (Fig.2)

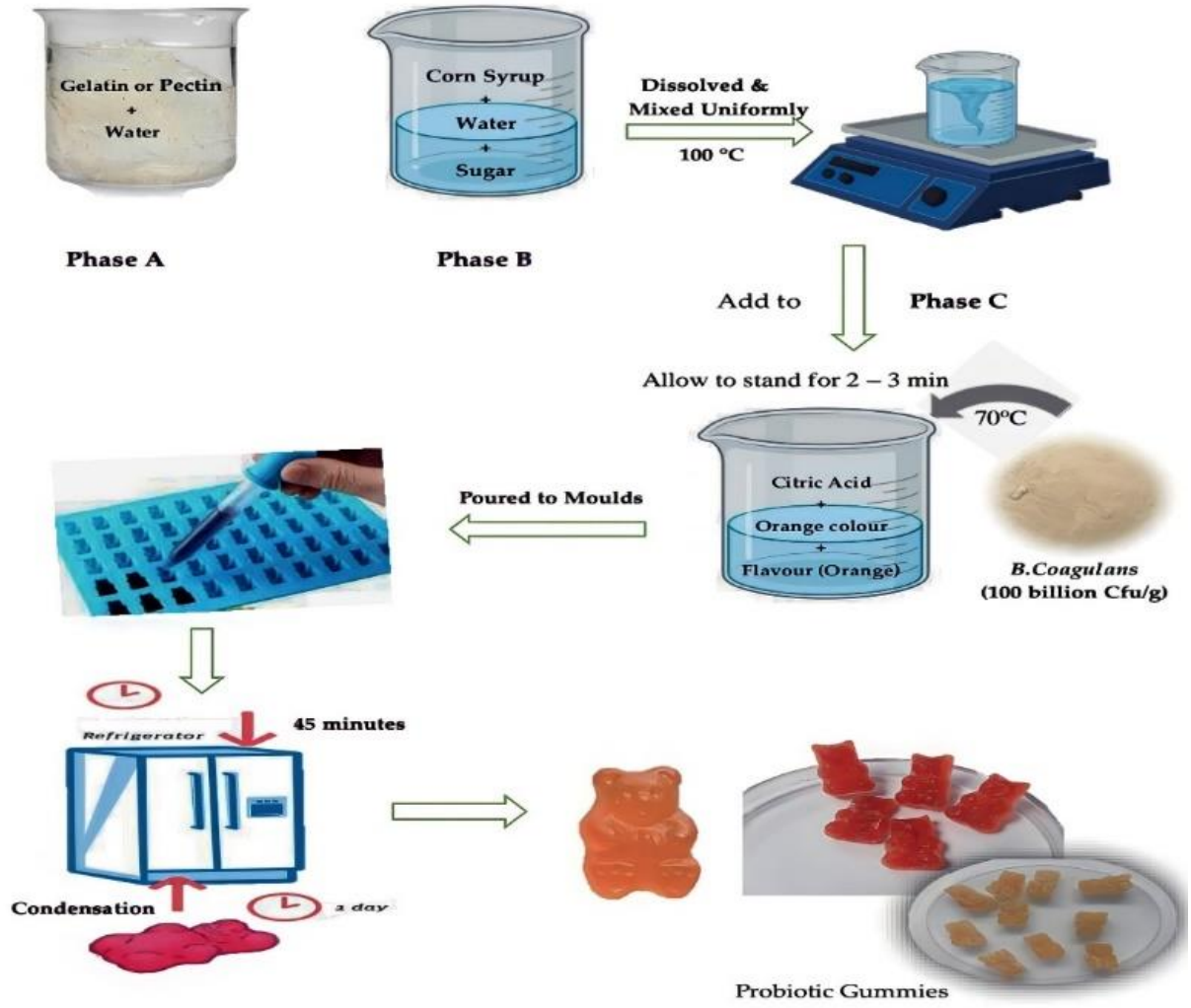



**Fig.2.**Schematic Representation for Preparation of Probiotic gummies

After every time interval for the stability studies, 1.0 g of sample (Probiotic Gummies containing *B. coagulans*) was thoroughly mixed in sterile saline (0.9% NaCl, w/v) and then incubated in water bath for 30 min at 75 °C, followed by immediate cooling to below 45 °C. This suspension was further serially diluted in sterile saline and the viable count was enumerated by plating on glucose yeast extract agar (HiMedia, Mumbai, India) by pour plate method [12]. The plates were incubated at 37 °C for 48–72 h. Total Yeast & Mold count was determined each analysis was performed in triplicate. Average mean of spore viable counts are expressed in $\log^{10}$ Cfu.

The Proximal composition of Gummy supplements with *B.coagulans* was analyzed by the following official method of the Association of Official Analytical Chemists (AOAC) [13].The stability studies were carried out for the Probiotic Gummies F1 and F2 formulations at 25 ± 2°C, 60 % ± 5% RH for six months. [14]

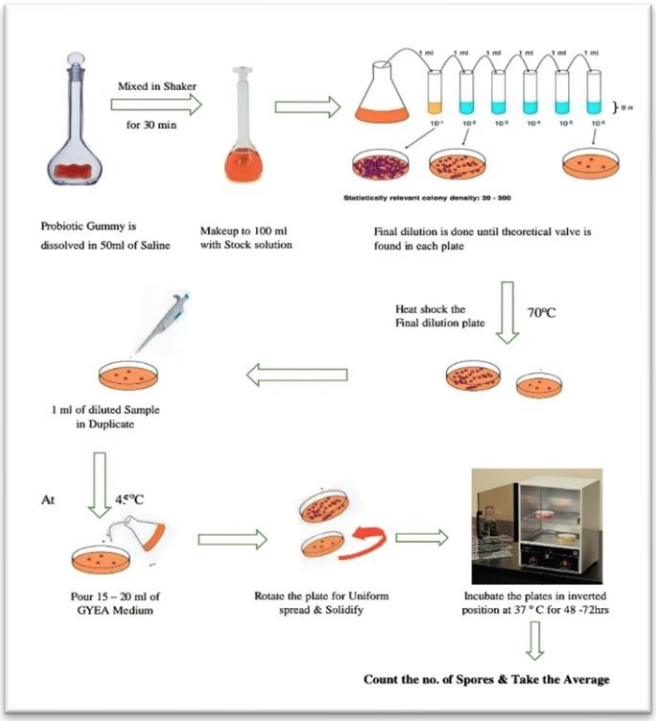



**Fig.3.** Schematic Representation of TVSC Plate for Probiotic gummies

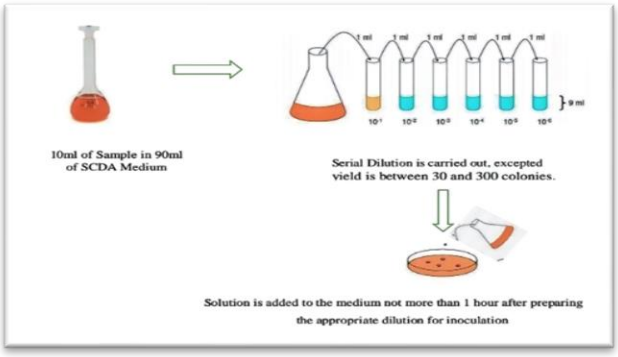
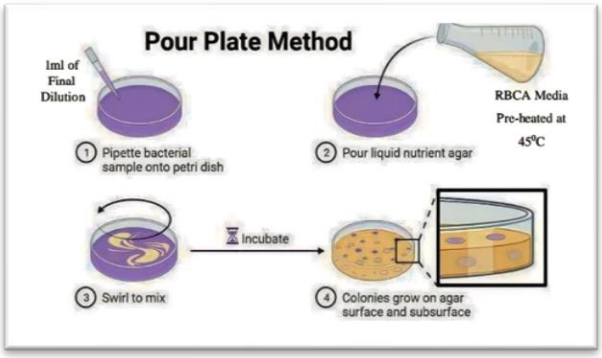



**Fig.4 (A).** Preparation of TYMC Plates for Probiotic Gummies




**(B).** Preparation of TYMC Plates by Pour plate Method for Probiotic Gummies

## RESULTS & DISCUSSIONS

Two different formulations were designed using different gelling agents with the help of optimization studies of the ingredients. *B. coagulans*, a probiotic, is incorporated into gummies. (100 billion Cfu/g), wherein Sugar (Sucrose) contributes 40% of the weight of the gummies, Gelatin and Pectin were used as gelling agents, (F1 & F2). Corn syrup gives sweetness to the gummies Citric acid acts as a preservative; and coloring & flavoring agents give the gummies an attractive look and a pleasant taste while consuming them. Each Probiotic gummy weighs about 2.0g ±0.25g and contains NLT 500 million spores/gummy (Fig.5)

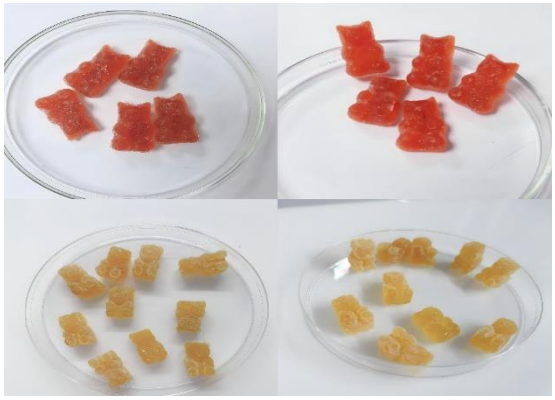


**Fig.5.** Probiotic gummies (F1 & F2)

### Evaluation Parameters for Probiotic Gummies

### a. Determination of Physical & Chemical Parameters

Physical & Chemical Parameters for probiotic gummies were evaluated. Odour and colour of Probiotic Gummies was evaluated. It was found that Gummies has Orange colored, Pleasant Orange Odour and Orange flavored and also the gummies are water soluble in nature. (Table.1)

**Table.1.** Organoleptic Properties of Probiotic Gummies

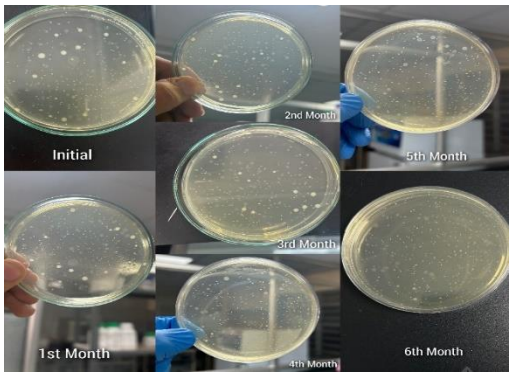
| **Product Name:** Probiotic Gummies containing *Bacillus coagulans* -100 Billion cfu/g | | | |
|---|---|---|---|
| **Sl.no** | **Parameters** | **Specification** | **Results** |
| **A** | Colour | Orange Colour | Complies |
| | Odour | Pleasant Orange Odour | Complies |
| | Taste | Orange Flavour | Complies |
| **B** | Water Solubility Test | NLT 50% | 80% |

### b. Determination of Microbial Parameters

### i. Total Viable Spore Count

TVSC is calculated with GYEA medium and the results are noted down with the help of microbial plate counts of $10^6$ and $10^7$ and it's expressed in Cfu /gummy using the formula. (Fig.6)

Viable Spore per gummy = Average number of colonies formed X dilution factor X 100



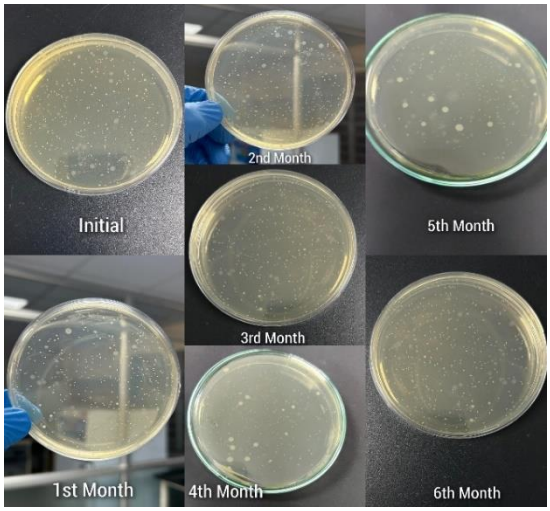



**Fig.6.** TYMC Plate count of Probiotic Gummies (F1 & F2)

**Table.2.** TVSC Calculation for Probiotic Gummies (F1 & F2)

| Time (month) | $Log_{10}$ Cfu /gummy | | Viability (%) | |
|---|---|---|---|---|
| | F1 | F2 | F1 | F2 |
| **0** | 8.7323 | 8.7160 | 100 | 100 |
| **1** | 8.7160 | 8.7160 | 99.8 | 100 |
| **2** | 8.7160 | 8.7075 | 99.8 | 99.9 |
| **3** | 8.7242 | 8.7075 | 99.9 | 99.9 |
| **4** | 8.7242 | 8.6989 | 99.9 | 99.8 |
| **5** | 8.7075 | 8.7075 | 99.7 | 99.9 |
| **6** | 8.7160 | 8.6989 | 99.8 | 99.7 |

## ii. Total Yeast & Mold Count

TYMC is calculated with GYEA medium and the results are noted down with the help of microbial plate counts of $10^1$ and $10^2$ and it's expressed in Cfu /gummy using the formula.

**Total Yeast and Mold Count (TYMC) =** Average number of colonies x Dilution factor (Cfu/g)

**Table.3.** TYMC Calculation for Probiotic Gummies (F1)

| Time (month) | Dilution | | No. of Colonies | | Cfu /gummy |
|---|---|---|---|---|---|
| **0** | $10^{-1}$ | $10^{-2}$ | 00 | 00 | < 10 |
| **1** | $10^{-1}$ | $10^{-2}$ | 00 | 00 | < 10 |
| **2** | $10^{-1}$ | $10^{-2}$ | 00 | 00 | < 10 |
| **3** | $10^{-1}$ | $10^{-2}$ | 00 | 00 | < 10 |
| **4** | $10^{-1}$ | $10^{-2}$ | 00 | 00 | < 10 |
| **5** | $10^{-1}$ | $10^{-2}$ | 00 | 00 | < 10 |
| **6** | $10^{-1}$ | $10^{-2}$ | 00 | 00 | < 10 |

**Table.4.** TYMC Calculation for Probiotic Gummies (F2)

| Time(month) | Dilution | | No. of Colonies | | Cfu /gummy |
|---|---|---|---|---|---|
| **0** | $10^{-1}$ | $10^{-2}$ | 00 | 00 | < 10 |
| **1** | $10^{-1}$ | $10^{-2}$ | 00 | 00 | < 10 |
| **2** | $10^{-1}$ | $10^{-2}$ | 00 | 00 | < 10 |
| **3** | $10^{-1}$ | $10^{-2}$ | 00 | 00 | < 10 |
| **4** | $10^{-1}$ | $10^{-2}$ | 00 | 00 | < 10 |
| **5** | $10^{-1}$ | $10^{-2}$ | 00 | 00 | < 10 |
| **6** | $10^{-1}$ | $10^{-2}$ | 00 | 00 | < 10 |

## c. Nutritional Fact of Probiotic Gummies

The Proximal composition of Gummy supplements with *B.coagulans* was analyzed by the following official method of the Association of Official Analytical Chemists (AOAC).The results of the Nutritional Facts of Probiotic Gummies (Table.5)

The presence of moisture in the gummies was analyzed by the moisture-vacuum oven method and the results varied by 14.6% to 16.28% within the formulations (F1 and F2). Similarly, the Carbohydrate and Total Sugar content in the formulations F1 and F2 varied b/w 75.1% to 82.76% w/w and 65.4% to 79.91% w/w. The content of fat & protein in the probiotic gummies with *B.coagulans* varied from 0.03 % to 0.78 % and 9.9 % to < 1% respectively The energy valve of gummies varied from 338 kcal/100gm to 340 kcal/100gm.The data of the nutritional study suggested that

*B.coagulans* was found to be stable in the gummies with different nutritional profiles.

**Table.5.** Nutritional Study Data of Probiotic Gummies

| Sl.no | Tests | Unit | Results | |
|---|---|---|---|---|
| | | | F1 | F2 |
| 1.1 | Moisture - Vacuum oven method | % w/w | 14.6 | 16.28 |
| 1.2 | Fat | % w/w | 0.03 | 0.78 |
| 1.3 | Protein | % w/w | 9.9 | < 1 |
| 1.4 | Carbohydrates | % w/w | 75.1 | 82.76 |
| 1.5 | Energy | Kcal | 340 | 338.1 |
| 1.6 | Total Sugar | % w/w | 65.4 | 79.91 |

## d. Stability Studies on Probiotic Gummies

The stability studies were carried out for the Probiotic Gummies F1 and F2 formulations at 25 ± 2°C, 60 % ± 5% RH for six months. Initially, the viability of gummies of F1 & F2 was found to be 100%, respectively, in both formulations. During the study period, the probiotic content in the formulations F1 & F2 was found to be 99.8% and 100% at the end of 1st month, respectively. The Probiotic content in the formulations F1& F2 was found to be 99.8% & 99.9%, respectively, at the end of the 2nd month. During the study period, the Probiotic content in the formulations F1& F2 was found to be 99.9% respectively, at the end of the 3rd month. At the end of the study, the Probiotic content in F1 & F2 was found to be 99.8% and 98.8%, respectively, in both formulations. On average, the content of probiotics in gummies in the formulations F1 & F2 was found to be 100% initially; at the 6th month, the probiotic content was found to be 99.8% stable in the formulated gummies. There were no significant differences found in the probiotic content during the stability study. This indicates that Probiotic Gummies are stable under storage conditions. Gummies were stored in an airtight container and there were no significant changes in colour or appearance found during the stability study period

**Table.6.** Criteria required to carry out Stability Studies for Probiotic Gummies

| | |
|---|---|
| **Product :** Probiotic Gummy<br><br>**Strain:** *Bacillus coagulans*<br><br>(F1 & F2)<br><br>**Batch no:** PZ /PG-BC/501<br><br>PZ/PG-BC/502<br><br>**Mfg. Date:** 20/12/2022 | **Sample Pack:**<br><br>Kept in self -sealing double polythene bag enclosed.<br><br>**Storage:** 25 ± 2°C, 60 % ± 5% RH<br><br>**Quantity:** About 16 g per analysis or 8 gummies |
| **Test Performed**<br><br>1.Colour<br><br>2.Flavour<br><br>3.Assay:<br><br>A. Total Viable Spore Count<br><br>B. Total Yeast & Mold Count<br><br>C. Viability % | **Frequency of Testing**<br><br>At intervals of<br><br>1,2,3,4,5& 6months |

**Table.7.** Stability Data of Probiotic Gummies (F1 & F2)

| Period of Testing | Colour | Flavour | Assay | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | A | | B | | C | |
| | | | F1 | F2 | F1 | F2 | F1 | F2 |
| Initial | Orange | Orange | 540 | 520 | <10 | <10 | 100 | 100 |
| 1st Month | Orange | Orange | 525 | 515 | <10 | <10 | 99.8 | 100 |
| 2nd Month | Orange | Orange | 520 | 515 | <10 | <10 | 99.8 | 99.9 |
| 3rd Month | Orange | Orange | 525 | 510 | <10 | <10 | 99.9 | 99.9 |
| 4th Month | Orange | Orange | 525 | 505 | <10 | <10 | 99.9 | 99.8 |
| 5th Month | Orange | Orange | 510 | 510 | <10 | <10 | 99.7 | 99.9 |
| 6th Month | Orange | Orange | 515 | 505 | <10 | <10 | 99.8 | 99.8 |
| LIMITS | Orange | Orange | NLT 500 Million Spore /gummy | | NMT 100 cfu/g | | NLT 98 % | |

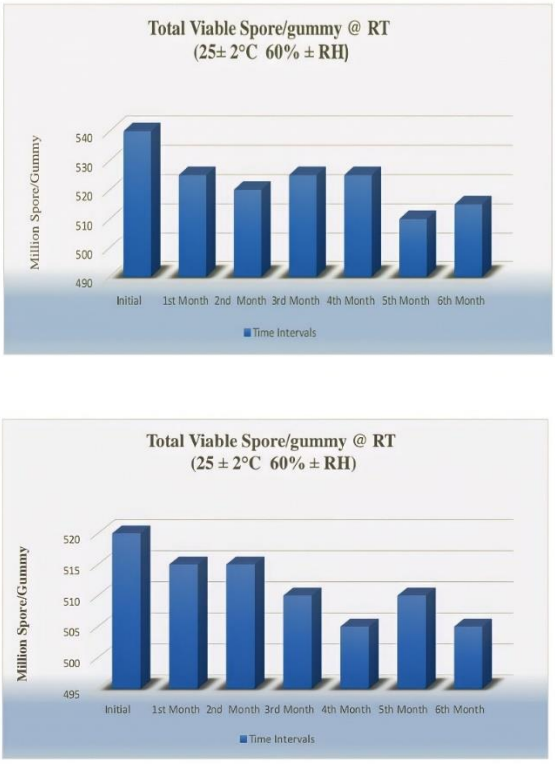



**Fig.7.** Viability Count of Probiotic Gummies (F1 & F2)

## CONCLUSION

Probiotic Gummies were successfully prepared by using *B.coagulans* as a Probiotic with the help of different gelling agents like Gelatin and Pectin. Two different formulations were prepared with the help of Optimization data using sucrose, gelatin and pectin as the base for the preparation of gummies. All the prepared probiotic gummies were subjected to various evaluation parameters like pre-formulation studies, microbial analysis, nutritional facts and Stability data. Microbial parameters, including Total Viable Spore Count (TVSC), Total Yeast & Mold count (TYMC) and Pathogen testing, were carried out and they comply within the limits. Nutritional content in the formulation was analysed and the results were determined and depicted for various constituents like Carbohydrate and Total Sugar content in the formulations, which varied from 75.1% to 82.76% and 65.4% to 79.91% w/w. Fat and protein in the probiotic gummies with *B.coagulans* varied from 0.03 % to 0.78 % and 9.9 % to < 1%, respectively. The energy value of gummies varied from 338 kcal /100 g to 340 kcal/100gm. Short-term stability Studies of the formulations indicate that there are no significant changes in physical characteristics, viable count, traces of yeast & molds and pathogens after 180 days of storage at 25±2º C with 60±5% RH.

## ACKNOWLEDGEMENT

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## Conflict of interests

The author(s) disclose that finical support for the research described manuscript was provided by ProZye Healthcare, Plot no 123 8th Cross Hebbal Industrial Area, Hebbal Mysore, Karnataka, India. Mr. Mohammed Swaleh is the founder and Managing Director of ProZye Healthcare. All authors approved the final version of the manuscript.

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Research Article

# DESIGN AND DEVELOPMENT OF VITAMIN 'A' STABILIZATION BY DIFFERENT TECHNIQUE

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## ABSTRACT:

Vitamin A Palmitate (VAP) contains retinol and palmitic acid, which are essential to the body. But it is a light-sensitive molecule that undergoes degradation when exposed to UV light. The purpose of this study was to prepare a stabilised VAP powder using Spray drying and the encapsulation technique. For spray drying, an emulsion of VAP was prepared using maize starch and maltodextrin with tween 80 as an emulsifier and the resulting emulsion was spray dried.
For encapsulation, VAP was mixed with MCC and sorbic acid as a preservative and the mixture was lyophilized.
The stabilised powder contains 35% VAP and was produced using different concentrations of wall materials. The prepared powder was evaluated for their physical properties, drug content, *in-vitro* drug release and SEM study. The result showed that the obtained powder is nearly spherical in shape, with a particle size range of 1–14 µm. The drug content of different batches was found to be within an acceptable range. The drug release study showed 87.41% to 95.8% of drug release from stabilised powder at the end of 60 minutes. The formulations were kept for a 3-month stability study as per ICH guidelines and found to be stable.

**Key words:** Vitamin A Palmitate, Spray drying, Encapsulation, Lyophilization, Stability studies.

## INTRODUCTION:

Vitamins are vital micronutrients that are involved in many biological functions in the body. An adequate intake of Vitamins is known to maintain normal health and immunity, help regulate metabolism in the body and in some cases to prevent chronic diseases.
Vitamins are categorised into two types based on their solubility in water or fat.

➢ Fat soluble Vitamins A, D, E and K.

➢ Water-soluble Vitamins B and C.

Vitamin A is an essential nutrient needed in small amounts for the normal functioning of the visual system and the maintenance of cell function for growth, epithelial integrity, red blood cell production, immunity and reproduction.[1]

Recommended Dietary Allowances (RDAs) for Vitamin A.

| Age | Male | Female | Pregnancy | Lactation |
|---|---|---|---|---|
| Birth to 6 months | 400 mcg RAE | 400 mcg RAE | | |
| 7-12 months | 500 mcg RAE | 500 mcg RAE | | |
| 1-3 years | 300 mcg RAE | 300 mcg RAE | | |
| 4-8 years | 400 mcg RAE | 400 mcg RAE | | |
| 9-13 years | 600 mcg RAE | 600 mcg RAE | | |
| 14-18 years | 900 mcg RAE | 700 mcg RAE | 750 mcg RAE | 1200 mcg RAE |
| 19-50 years | 900 mcg RAE | 700 mcg RAE | 770 mcg RAE | 1300 mcg RAE |
| 54+ years | 900 mcg RAE | 700 mcg RAE | | |

RAE: Retinol Activity Equivalents [2]

### Vitamin A Deficiency[3]: -

It causes

a) Night blindness.
b) Xeropthalmia or dry eyes.
c) Reproductive functions may also be affected by Vitamin A deficiency.
d) Compromised Immune system.
e) Poor dental Health.

## Causes for Vitamin A instability:

Vitamin A is sensitive to light, particularly ultraviolet (UV) light. When Vitamin A is exposed to light, the energy from the light can break down the double bonds in the molecule, resulting in the formation of free radicals. These reactions can cause the degradation of Vitamin A and reduce its effectiveness.

Exposure to light can cause the degradation of Vitamin A, leading to a loss of its biological activity. This sensitivity is due to the chemical structure of Vitamin A, which contains a conjugated double bond system that can undergo photochemical reactions.[4]

Vitamin A is sensitive to heat and can undergo degradation when exposed to high temperatures for extended periods. Heat can cause the breakdown of the molecular structure of vitamin A, leading to a loss of its nutritional value. The exact temperature and duration required to degrade Vitamin A may vary, but it generally begins to degrade significantly at temperatures above 60°C. So, we aim to prepare Vitamin A in a stabilised form that has a reasonably high shelf life, using different techniques such as Spray drying and Encapsulation.

## MATERIALS AND METHODS

For spray drying technique

Vitamin A Palmitate, Vitamin E as anti-oxidant, Colloidal silicon dioxide as glidant, Maize starch coating agent, Maltodextrin as bulking agent, Tween 80 as emulsifier.

For encapsulation technique

Vitamin A Palmitate, Vitamin E as anti-oxidant, Micro crystalline cellulose as bulking agent, Sorbic acid and sodium benzoate as preservatives, Aerosil as glidant, Alginate as emulsifying agent, Tween 80 as emulsifier.

## Preformulation studies

- Organoleptic properties
- Solubility analysis:10mg of VAP dissolve in various solutions like IPA, ethanol, methanol, chloroform, ethyl ether.

## Determination of λ max

1mg of VAP were dissolved in 10ml of IPA and the maximum absorption was analysed between 200-400 nm using UV-Visible spectrophotometer.

## Preparation of Standard calibration curve of VAP

100mg of VAP were dissolved in 100ml IPA solution to get the concentration of 1mg/ml. From the above solution pipette out 10ml and make up to 100ml using IPA solution to get 100µg/ml concentration. And pipette out 0.1, 0.2, 0.3, 0.4, 0.5, 0.6 and 0.7 ml and make up to 10ml using IPA to get 1, 2, 3, 4, 5, 6 and 7 µg/ml and analysed against a blank (IPA) by using the UV -Visible spectrophotometer.

## Compatibility study using FT-IR

In the preparation of stabilized Vitamin-A, polymer may interact as they are in close contact with each other, which could lead to the instability of drug. FTIR spectroscopy helps to identity of the drug and polymer interaction. The pure drug, pure polymer, physical mixture of drug, polymer and other excipients were prepared and scanned from 4000-400$cm^{-1}$ in FTIR spectrophotometer the IR spectrum of pure VAP and formulated VAP powder were recorded by FTIR spectrophotometer.[5]

## Method for preparation of stabilized VAP powder

## Preparation of stabilised Vitamin A by spray dryer technique.

| Sl no | Ingredients | F 1 | F 2 | F 3 |
|---|---|---|---|---|
| 1 | Vitamin A palmitate | 35 | 35 | 35 |
| 2 | Vitamin E | 2 | 2 | 2 |
| 3 | Colloidal silicon dioxide | 20 | 20 | 20 |
| 4 | Maize starch | 20 | 15 | 10 |
| 5 | Maltodextrin | 18 | 23 | 28 |
| 6 | Tween 80 | 5 | 5 | 5 |

**Quantities % w/w**

Vitamin A Palmitate was heated to 50$^{O}$C, tween 80 and vitamin E was mixed and kept aside. Water was boiled and maintained at 60-65$^{O}$C. Colloidal silicon dioxide, maize starch and maltodextrin was mixed and kept aside. VAP and tween 80 mixture was added to water with constant stirring to o/w emulsion. To the obtained emulsion, colloidal silicon dioxide, maize starch and maltodextrin were added with constant stirring and required amount of water was added later. Obtained solution is spray dried with inlet temperature of 110-130$^{O}$C and outlet temperature of 55-60$^{O}$C at 12,000 rpm. The product obtained is stored in sealed container in a black cover.

## Preparation of stabilised VAP powder by encapsulation

Dissolve sorbic acid in water, boil and add sodiumbenzoate, alginate and mix well, this solution was added to the MCC. VAP, Vitamin E and Tween 80 was mixed separately and kept aside. The obtained emulsion of VAP, VE and Tween 80 were added to the MCC mixture with constant stirring, followed by addition of Aerosil. Lyophilize the obtained product. Check the moisture content of the product after 5-6 hrs, continue lyophilization till the moisture content is not more than 3%.

| Sl no. | Ingredients | F1 | F2 | F3 |
|---|---|---|---|---|
| 1 | Vitamin A palmitate | 35 | 35 | 35 |
| 2 | Vitamin E | 2 | 2 | 2 |
| 3 | Micro crystalline cellulose (MCC) | 50 | 55 | 60 |
| 4 | Sorbic acid | 0.5 | 0.5 | 0.5 |
| 5 | Sodium benzoate | 0.5 | 0.5 | 0.5 |
| 6 | Aerosil | 3 | 3 | 3 |
| 7 | Alginate | 3 | 3 | 3 |
| 8 | Tween 80 | 1 | 1 | 1 |

**EVALUATION OF THE PREPARED STABILISED VAP POWDER**

## Percentage yield

$$= \frac{weight\ of\ prepared\ VAP\ powder}{total\ weight\ of\ drug\ and\ polymer} \times 100$$

## Drug content:

## HPLC analysis[6]:- Chromatographic conditions

The separation was carried out on RP- HPLC system (Shimadzu, UV-1900i Japan) with HPLC pump, photo diode array (PDA) detector, LabSolutions software and Luna, 5u C18, column (250mmx4.6mm)

## Preparation of mobile phase for VAP

The mobile phase was prepared by the mixture of Methanol, Acetonitrile and Water in the ratio of 750 : 225 : 25 v/v (HPLC grade) and was filtered through 0.45 µm membrane filter (Milli-pore, USA) and degassed.

## Preparation of standard VAP solution:

Accurately weighed and transferred about 100 mg of VAP into a 50 ml clean, dry amber coloured volumetric flask and made up to the volume with hexane to get concentration 2 mg/ml. From the above solution 1ml was further diluted to 50ml with methanol.

## Preparation of sample VAP solution:

Equivalent to 100mg of weighed VAP powder were suspended in the 50 ml volumetric flask and made up to the volume with hexane. From the above solution 1ml was further diluted to 50 ml with methanol.

## Procedure:

Mobile phase was pumped into the column at a flow rate of 2.0 ml/min. The volume of the injection loop was set to 20 µl prior to the auto-injection of standard and sample solution and the column was equilibrated for at least 30 min with the mobile phase flowing through the system. The detection was monitored at 325 nm for VAP and the run time was 15 min. Recorded the area of the chromatogram. The drug content was calculated by using the formula,

$$\text{Assay} = \frac{Sample\ area}{Standard\ area} \times \frac{Standard\ weight}{Standard\ dilution} \times \frac{Sample\ dilution}{Sample\ weight} \times Standard\ purity$$

## Micromeritic study

The flow property of the powder was studied by determining the parameters like angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio.

- **Angle of repose:** tan θ= h/r or θ=tan-1 (h/r)

where, h = height of pile
r = radius of the base of the pile
θ= angle of repose

$$\text{Bulk density} = \frac{\textit{weight of the VAP powder } (W)}{\textit{Initial volume occupied by the powder } (V0)}$$

$$\text{Tapped density} = \frac{\textit{weight of the powder } (W)}{\textit{final volume occupied by the powder } (vf)}$$

$$\text{Hausner's ratio} = \frac{\textit{Tapped density}}{\textit{Bulk density}}$$

$$\text{Carr's index } C_i = \frac{\textit{Tapped density} - \textit{Bulk density}}{\textit{Tapped density}} \times 100$$

## Scanning electron microscopy (SEM)[7]

To evaluate physical surface and morphology of stabilized powder like size and shape was analysed using scanning electron microscope.

## *IN-VITRO* DRUG RELEASE STUDY[8]

The *in-vitro* dissolution studies were carried out using USP type -II Dissolution apparatus. VAP stabilised powder was filled in tea bag and tea bag were placed in dissolution apparatus containing 900ml 7.4 pH phosphate buffer which was maintained at 37±0.5$^{O}$C and at a stirring speed of 50 rpm. 5ml samples were withdrawn at predetermined time intervals and same volume of fresh medium was replaced into the basket. Sample was withdrawn at time intervals of 5, 10, 20, 30, 40, 50 and 60 min. The concentration of drug released was estimated by using UV spectrophotometer at λ max 325nm.

## STABILITY STUDIES

In order to determine the change in the parameters like physical appearance, drug content, *in-vitro* drug release profile on storage, stability studies of optimized batch were carried out at short term and accelerated storage condition at temperature 25±2º C with 60±5% RH and 40±2$^{O}$C with 75±5% RH in a stability chamber for 90 days. Sample were withdrawn after 30, 60, 90 days evaluated for changes in physical appearances and drug content.

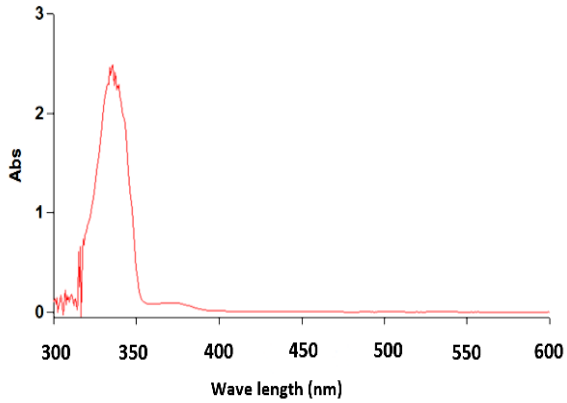
## RESULTS AND DISCUSSION

**Pre-formulation studies of VAP.**

Organoleptic characteristics & Solubility of VAP.

| Properties | Reported | | Observed |
|---|---|---|---|
| Appearance | Yellow viscous oil | | Yellow viscous oil |
| Odour | Odour | | Mild odour |
| Solubility | Ethanol | Soluble | Soluble |
| | Methanol | Soluble | Soluble |
| | IPA | Soluble | Soluble |
| | Chloroform | Soluble | Soluble |
| | Ethyl ether | Soluble | Soluble |
| | Water | Insoluble | Insoluble |
| | Glycerol | Insoluble | Insoluble |

**Determination of λ max**




**λ max of VAP in IPA**

Solution of VAP (100 µg/ml) was prepared using IPA and this solution was scanned for absorbance 200-800 nm using UV spectrophotometer. As shown in fig. peak was obtained at 325 nm. The absorption maximum (λmax) was found 325 nm. This value

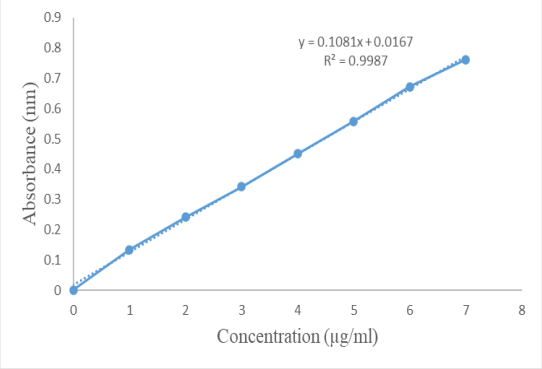
was selected for rest of the UV spectrophotometric analysis.

**Standard calibration plot**

| Sl. no | Concentration (µg/ml) | Absorbance ± SD* |
|---|---|---|
| **1** | 0 | 0 |
| **2** | 1 | 0.134±0.001 |
| **3** | 2 | 0.241±0.004 |
| **4** | 3 | 0.342±0.002 |
| **5** | 4 | 0.451±0.001 |
| **6** | 5 | 0.558±0.003 |
| **7** | 6 | 0.672±0.002 |
| **8** | 7 | 0.761±0.002 |

*All the Values represents are mean of 3 readings (n=3) ±SD- Standard deviation

**Standard calibration data of VAP**

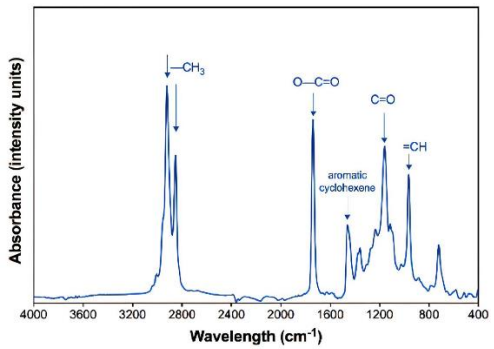



**Standard calibration plot of VAP**

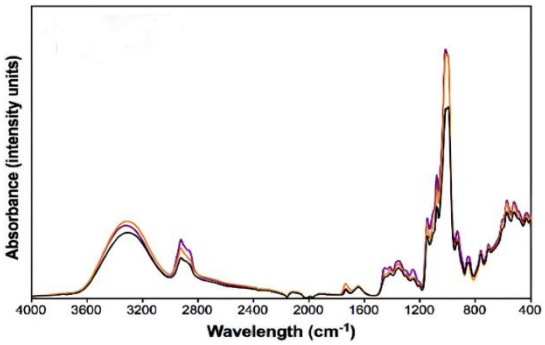
The drug solution of 1µg/ml - 7µg/ml was prepared using IPA and absorbance measured using UV spectrophotometer at the absorption maximum (λ max) 325 nm. The obtained absorbance data is plotted against the concentration of drug solution. Absorbance value remained linear and obeyed Beer's Lamberts law in the range of 0-7µg/ml with the slope value as y = 0.1081x + 0.0167 and R2 value of 0.9987.

**Compatibility studies using FT-IR.**

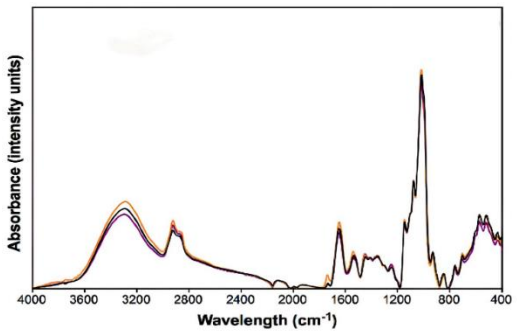
| Functional groups | Wavelength from 400 to 4000 $cm^{-1}$ | | | |
|---|---|---|---|---|
| | Vitamin A palmitate | Vitamin E | Spray dried product | Encapsulated product |
| **$CH_3$ stretching** | 2922 | 2864 | - | - |
| **C=O stretching** | 1739 | - | 1725 | 1640 |
| **-CO stretching** | 1350 | 1355 | 1372 | 1367 |
| **CH** | 2900 | - | 2905 | 2910 |
| **OH** | - | 3473 | 3475 | 3451 |
| **$CH_2$** | - | 1422 | 1428 | 1437 |




FTIR spectra of pure Vitamin A palmitate.




FTIR spectra of spray dried VAP powder




FTIR spectra of encapsulated VAP powder

The results of the IR spectrum of excipients and the drug VAP showed the presence of characteristic peaks very similar to those of the reference peaks reported previously. While the IR spectra of the drug and the drug-loaded particles showed no absence of new peaks or disappearance of the existing peak, which shows that there was no covalent interaction between the VAP and excipients and furthermore, the polymer did not alter the performance characteristics of drugs.

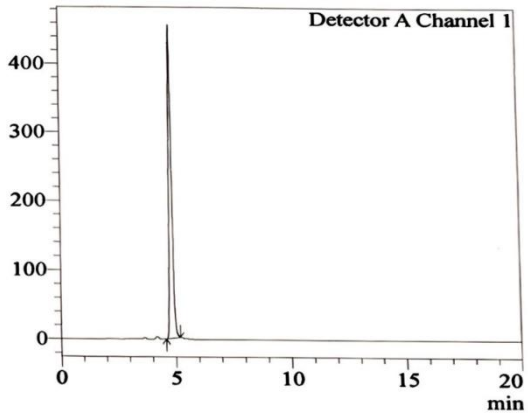
**Evaluation of VAP stabilised powder**

Percentage yield of VAP stabilised powder

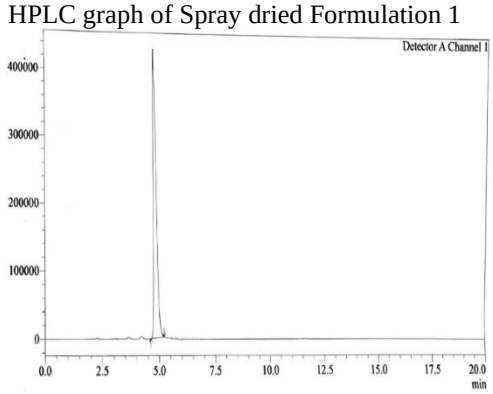
| Sl no. | Formulation | % yield w/w |
|---|---|---|
| **In spray dried technique** | | |
| **1** | F1 | 80.72 |
| **2** | F2 | 82.21 |
| **3** | F3 | 78.68 |
| **In encapsulation technique** | | |
| **1** | F1 | 91.26 |
| **2** | F2 | 95.05 |
| **3** | F3 | 92.10 |

**DRUG CONTENT DETERMINATION**

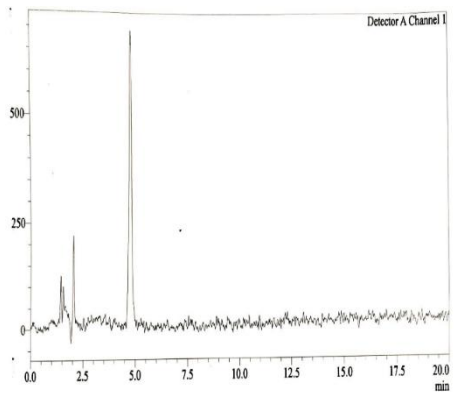
The drug content is determined using HPLC



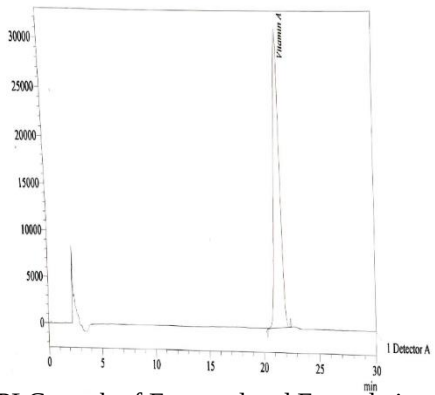

HPLC graph of Spray dried Formulation 1



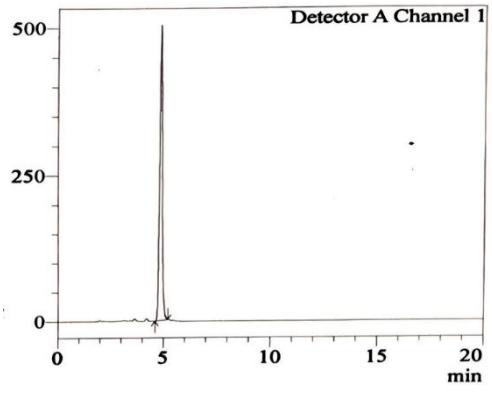

HPLC graph of Spray dried Formulation 2



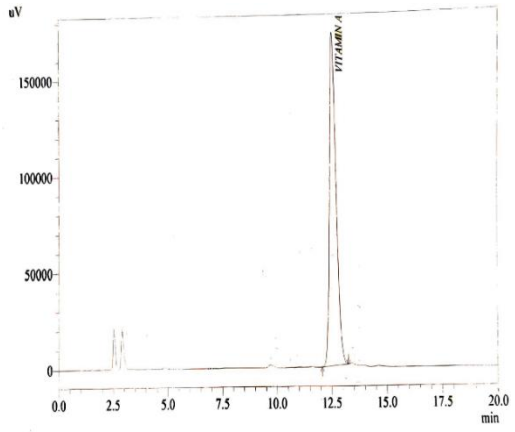

HPLC graph of Spray dried Formulation 3




HPLC graph of Encapsulated Formulation 1



HPLC graph of Encapsulated Formulation 2




HPLC graph of Encapsulated Formulation 3

| Formulations | Area of principle peak | Weight of sample (mg) | % Assay |
|---|---|---|---|
| **Spray dried technique** | | | |
| **F1** | 3480412 | 100.02 | 96.64 |
| **F2** | 3486872 | 99.59 | 97.41 |
| **F3** | 3479363 | 100.5 | 96.23 |
| **In encapsulation technique** | | | |
| **F1** | 3497253 | 99.57 | 97.31 |
| **F2** | 3584358 | 99.89 | 99.73 |
| **F3** | 3501213 | 99.38 | 98.01 |

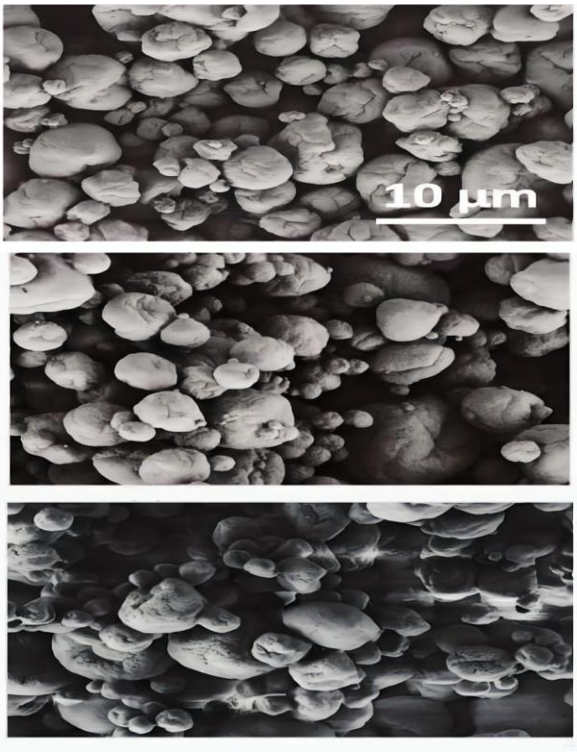
HPLC data of VAP stabilised powder.

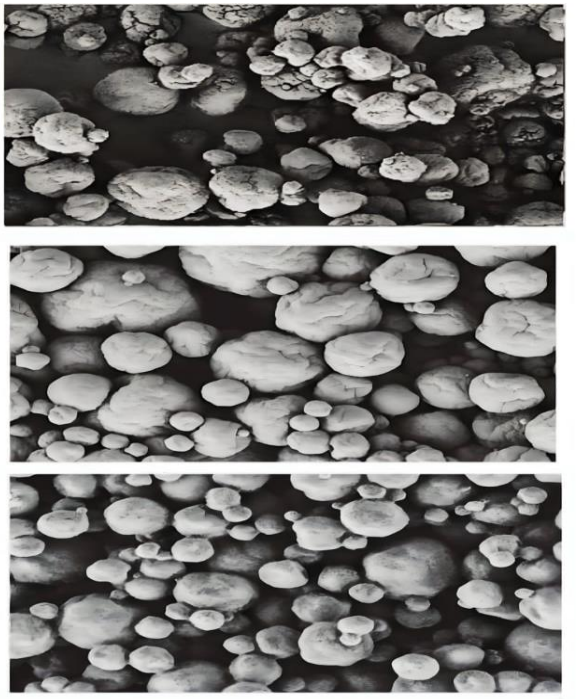
The drug content of VAP was determined using HPLC in both techniques. The drug content was found to be in the range of 96.23 to 97.41% in the spray drying technique and 97.31 to 99.73% in encapsulation technique.

## Micromeritic study

| Formulation code | Angle of repose ($\theta^O$) | Bulk Density (gm/ml) | Tapped Density (gm/ml) | Carr's index(%) | Hausner Ratio |
|---|---|---|---|---|---|
| **In spray drying technique** | | | | | |
| **F1** | 38.65 ±0.24 | 0.253 ±0.02 | 0.322 ±0.01 | 21.42±0.4 | 1.27 ±0.02 |
| **F2** | 37.95 ±0.31 | 0.243 ±0.01 | 0.307 ±0.01 | 20.84±0.2 | 1.26 ±0.04 |
| **F3** | 39.35 ±0.27 | 0.240 ±0.01 | 0.307 ±0.03 | 21.82±0.5 | 1.27 ±0.02 |
| **In encapsulation technique** | | | | | |
| **F1** | 32.61 ±0.18 | 0.465 ±0.02 | 0.540 ±0.02 | 13.83±0.6 | 1.16 ±0.03 |
| **F2** | 30.54 ±0.35 | 0.444 ±0.03 | 0.513 ±0.02 | 13.33±0.3 | 1.15 ±0.02 |
| **F3** | 31.38 ±0.23 | 0.416 ±0.02 | 0.487 ±0.01 | 14.57±0.4 | 1.17 ±0.02 |

## Scanning electron microscope





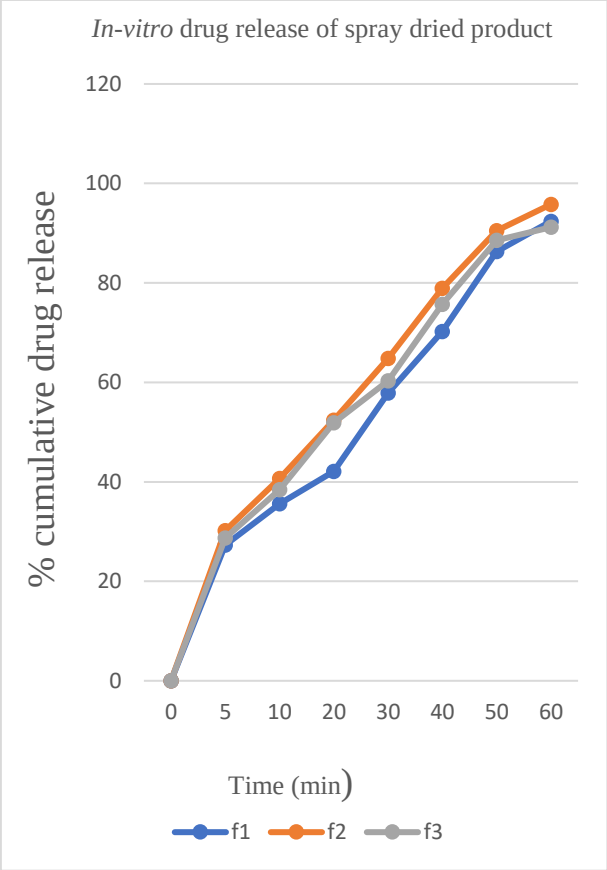
**SEM images of stabilised VAP powder by spray drying technique and encapsulated.**

The shape and surface morphology of the prepared VAP powder were observed by scanning electron microscopy. Scanning electron microscopy reveals that the stabilised VAP has a semi-spherical shape. Particle size distribution with a more frequent diameter in the range from 1 to 14 µm.

***In vitro* drug release study**

| Time (min) | Cumulative % drug release | | |
|---|---|---|---|
| | F1 | F2 | F3 |
| 0 | 0 | 0 | 0 |
| 5 | 27.3±0.12 | 30.2±0.21 | 28.7±0.20 |
| 10 | 35.6±0.15 | 40.7±0.15 | 38.4±0.11 |
| 20 | 42.1±0.13 | 52.4±0.14 | 51.9±0.16 |
| 30 | 57.9±0.17 | 64.8±0.12 | 60.3±0.13 |
| 40 | 70.2±0.20 | 78.9±0.14 | 75.7±0.13 |
| 50 | 86.3±0.18 | 90.5±0.15 | 88.6±0.11 |
| 60 | 92.4±0.17 | 95.8±0.16 | 91.2±0.20 |

**Percentage cumulative drug release data of stabilised VAP powder by spray drying technique from formulations F1, F2 and F3.**



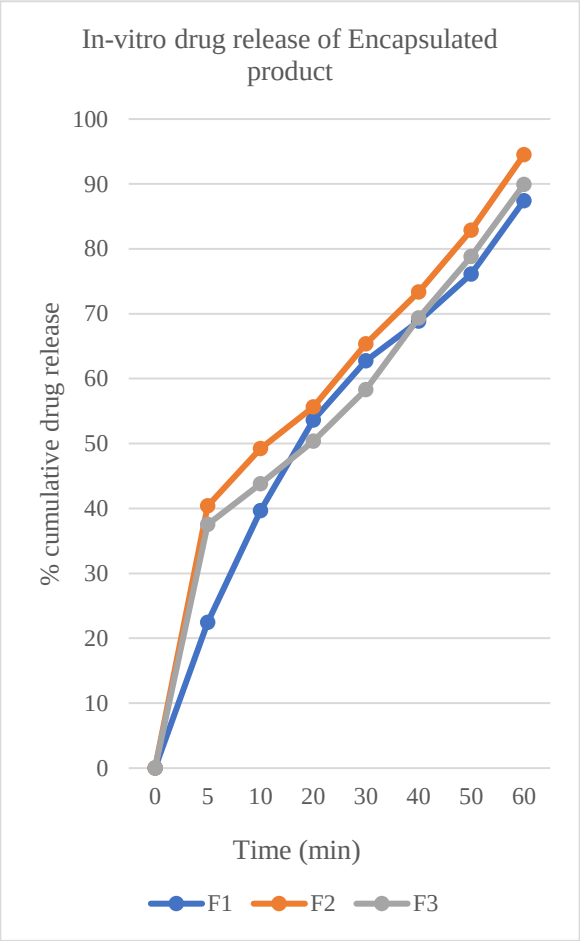

***In-vitro* drug release profile of VAP spray dried product**

The formulations F1, F2 and F3 containing spray dried VAP powder showed percentage drug realease of 92.4%, 95.8% and 91.2% respectively. In this the formulation F2 showed a better drug realease of 95.8% at the end of 60minutes.

| Time (min) | Cumulative % drug release | | |
|---|---|---|---|
| | F1 | F2 | F3 |
| 0 | 0 | 0 | 0 |
| 5 | 22.46±0.16 | 40.37±0.18 | 37.52±0.12 |
| 10 | 39.63±0.18 | 49.24±0.12 | 43.79±0.16 |
| 20 | 53.59±0.21 | 55.61±0.16 | 50.36±0.18 |
| 30 | 62.74±0.16 | 65.34±0.19 | 58.31±0.14 |
| 40 | 68.84±0.13 | 73.36±0.15 | 69.36±0.16 |

| | | | |
|---|---|---|---|
| **50** | 76.12±0.21 | 82.87±0.17 | 78.83±0.21 |
| **60** | 87.41±0.15 | 94.48±0.12 | 89.93±0.14 |

**Percentage cumulative drug release data of stabilised VAP powder by encapsulation technique from formulations F1, F2 and F3.**




***In-vitro* drug release profile of VAP encapsulated product**

The formulations F1, F2 and F3 containing encapsulated VAP powder showed percentage drug realease of 87.41%, 94.48% and 89.93% respectively. In this the formulation F2 showed a better drug realease of 95.8% at the end of 60minutes.

**Stability studies**

| Time (days) | Temperature & Humidity | Drug content (%) | | |
|---|---|---|---|---|
| | | F1 | F2 | F3 |
| **0** | - | 96.64 | 97.41 | 96.23 |
| **30** | **At 25±2ºC, 60±5% RH** | 95.85 | 97.02 | 95.26 |
| | **At 40±2ºC, 75±5% RH** | 95.51 | 96.93 | 95.11 |
| **60** | **At 25±2ºC, 60±5% RH** | 94.06 | 96.91 | 94.82 |
| | **At 40±2ºC, 75±5% RH** | 93.87 | 96.85 | 94.53 |
| **90** | **At 25±2ºC, 60±5% RH** | 93.51 | 96.17 | 93.58 |
| | **At 40±2ºC, 75±5% RH** | 93.04 | 95.97 | 93.12 |

**Stability studies of stabilised VAP powder of spray dried product**

| Time (days) | Temperature & Humidity | Drug content (%) | | |
|---|---|---|---|---|
| | | F1 | F2 | F3 |
| **0** | - | 97.31 | 99.73 | 98.01 |
| **30** | **At 25±2ºC, 60±5% RH** | 96.95 | 98.62 | 97.35 |
| | **At 40±2ºC, 75±5% RH** | 96.82 | 98.47 | 97.05 |
| **60** | **At 25±2ºC, 60±5% RH** | 95.72 | 97.59 | 96.58 |
| | **At 40±2ºC, 75±5% RH** | 95.47 | 97.22 | 96.11 |
| **90** | **At 25±2ºC, 60±5% RH** | 94.92 | 97.01 | 94.98 |
| | **At 40±2ºC, 75±5% RH** | 94.81 | 96.85 | 94.77 |

**Stability studies of stabilised VAP powder of encapsulated product**

## CONCLUSION

Spray drying and encapsulation techniques were used to stabilise Vitamin A. Three formulations were prepared by both techniques and evaluated. Micromeritic studies revealed that the prepared Vitamin A powder exhibited good flow. Scanning electron microscopy reveals that the stabilised VAP has a semi-spherical shape. The *in-vitro* drug release studies show that the obtained cumulative drug release (CDR) was found to be significant. The short-term stability studies of both technique products indicate that there are no significant changes in physical appearance and drug content after 90 days of storage. Altogether, the proposed techniques are feasible for the stabilisation of vitamin A and protection against degradation.

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# INTERNATIONAL JOURNAL OF COMMUNITY PHARMACY
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Authors should submit two hard copies of manuscripts and electronic version of the manuscript in a Compact Disc to the Editor. Authors also encouraged submitting a copy of manuscript to the Editor by electronic mail. Accepted papers will be processed further, if the papers are rejected, the decision will be communicated to the corresponding author but the manuscripts will not be returned.

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Abstract and Key words,
Introduction,
Materials and Methods,
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# International Journal of Community Pharmacy

*The Official Publication of ACPI*

## OBJECTIVES

- To organize into an association of all persons engaged in, interested in or connected with community pharmacy.
- To elevate and establish a standard of competence for community pharmacy.
- To develop and promote standards of education and training for community pharmacy.
- To develop and promote short term informal training programs for individuals interested in community pharmacy.
- To educate hospital trustees, Board of Directors, Board of Visitors and the public to understand that the practice of community pharmacy calls for special training and experience.
- To serve as a forum for exchange of ideas and experiences, and collection and dissemination of information in general community pharmacy.
- To spread the knowledge on the principles, practices, techniques and methods concerning community pharmacy.
- To promote and safeguard the status and the interest of community pharmacy and the interests of those engaged in it.
- To promote sponsor, submit, memorandums, petitions and representations to local, state, union and other authorities for better laws, and influence legislation which affect hospitals and other community pharmacy organizations.
- To organize conferences, seminars, meetings and discussions for the promotion and furtherance of the aims and objects of the ACPI.
- To undertake and bring out, publish, sell, distribute free or otherwise, edit, print and exhibit for sale, magazines publication, bulletins, books pamphlets and the like, in furtherance of the objects of the ACPI and in any event not for the purpose of carrying a trade there from but only for the purposes of furthering the objects of the ACPI.
- To raise any monies for the purpose of the ACPI by way of special subscriptions, membership or entrance fees, donations, special fees, loans or in any other manner on such terms and conditions as may be determined.
- To purchase, take on lease or in exchange, or otherwise acquire, any movable or immovable property, rights or privileges, which may be deemed necessary, expedient or desirable for any of the objects, of the ACPI.
- To accept from the Government, organizations, institutions and individuals, grants, donations, subscriptions, gifts bequests, endowments, special fees, etc, for the furtherance of the objects of the ACPI.
- To make from time to time, regulation and bye-laws for the control, conduct and regulation of the affairs of the ACPI.
- To confer Fellowships in community pharmacy on those who have done or are doing noteworthy service in the field of community pharmacy.
- To generally do all such other things as are incidental or conducive to the attainment of any or all of the above-mentioned objects.


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