RHEA

Autologous Bio-Active Molecules Enrich System

The smart way for Tissue Rejuvenation

SAFETRAN BioMedical Inc.

-Bio-Active Molecules Therapy(BαM) –

Unlocking Your Body's Self-Healing Power

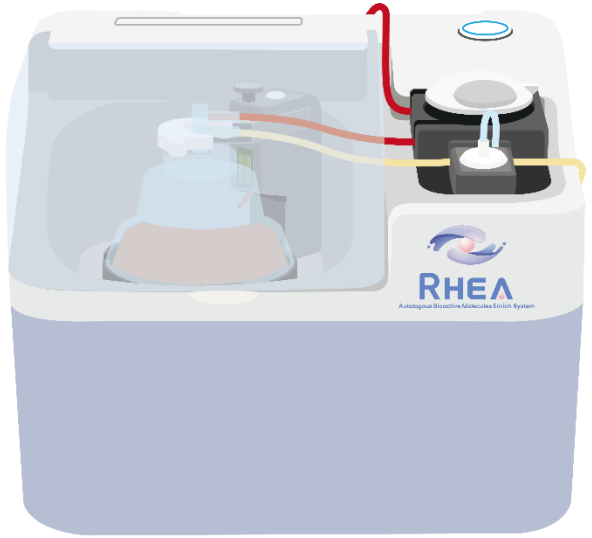
BaM is a highly concentrated, autologous biologic solution designed to accelerate tissue repair and restore physiological balance. By delivering supra-physiologic levels of essential healing factors, inducing Resident Macrophages and Resident Stem cells

BaM is the only therapy that enhances recovery and optimizes your body's natural regenerative potential.

Automatic Bio-Active Molecules Enrich System

BaM Collection	10-18ml
Interface	Single Button
Target Collection	Platelet& Plasma
Required Whole Blood	80 ml
Centrifuge Speed	1000~6000RPM±2%
Voltage Range	100~240VAC
Device Weight	6.5 kg max.
Device Dimension	W28 x D25 x H22 cm

Medical Device
Class IIa



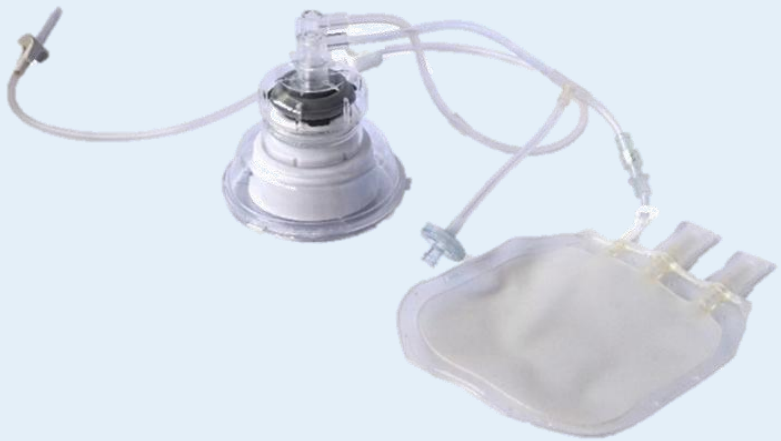
Core Competency of Rhea

Functional Close system

Prevent contamination

Latham Bowl Design

Maintain cell quality during separation



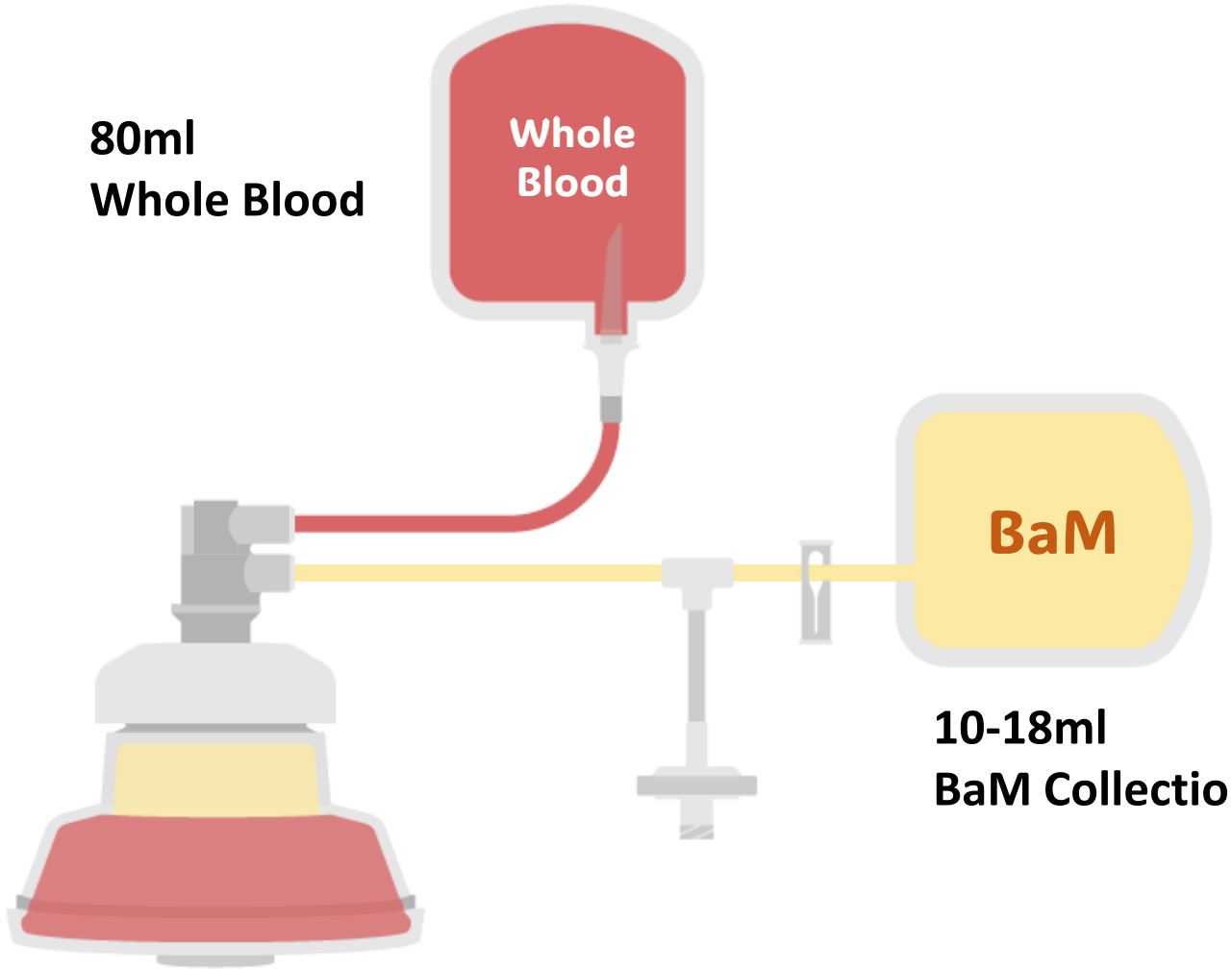
5 minutes Total Process!

Precision collection

Capturing Key Components through
Smart sensors and Software

Rhea’s Circuit

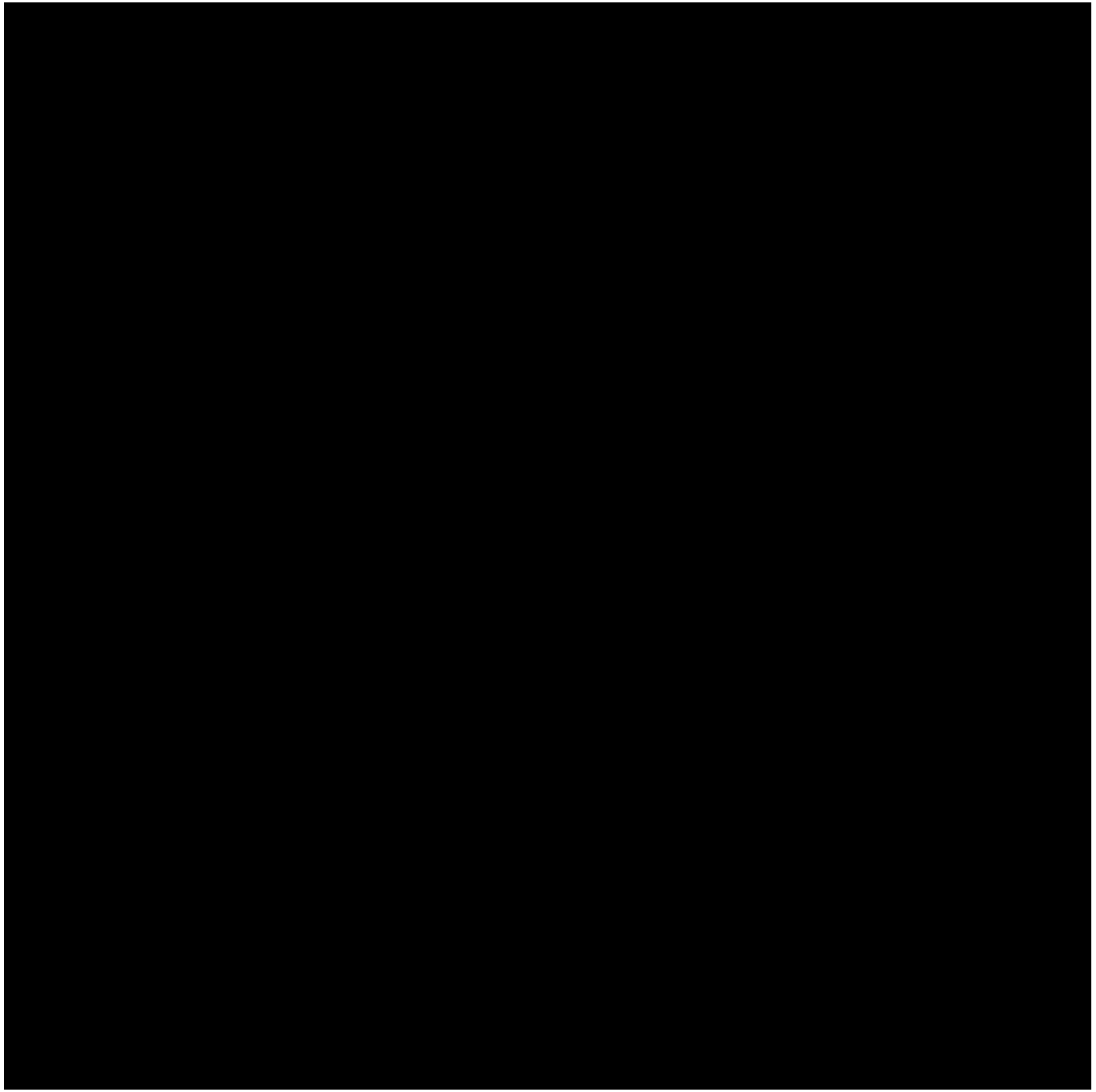
80ml
Whole Blood



10-18ml
BaM Collection

Patented Lathem bowl Design
To process Cell Separation

Rhea in Process



Rhea BαM Performance

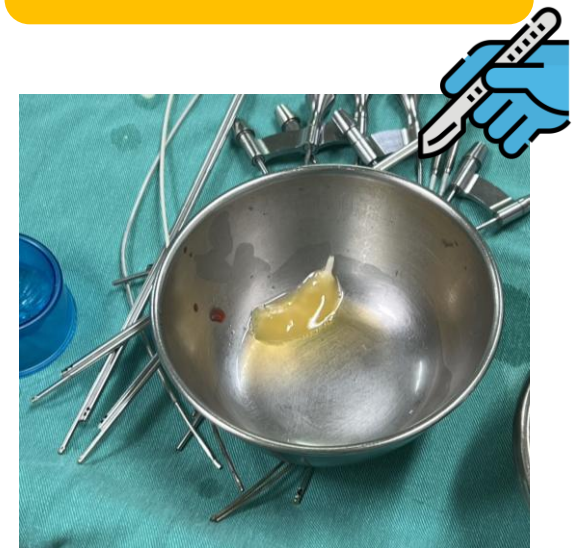
	A		B		C	
	WB	BαM	WB	BαM	WB	BαM
WBC	4.28	0.06	5.13	0.04	4.43	0.05
RBC	4.33	0.01	4.43	0.02	4.1	0
HCT	37.2	0.1	38.1	0.2	33.4	0
MPV Mean PLT Volume	7.1	7.3	7.01	7.03	7.2	7.64
PLT	182.7	357.8	252	509	212	406
PLTx		1.96x		2.02x		1.91x

MPV is consistent before and after centrifugation, indicating platelets are unharmed

Stable concentration rate

Forms of BaM

Gel Type

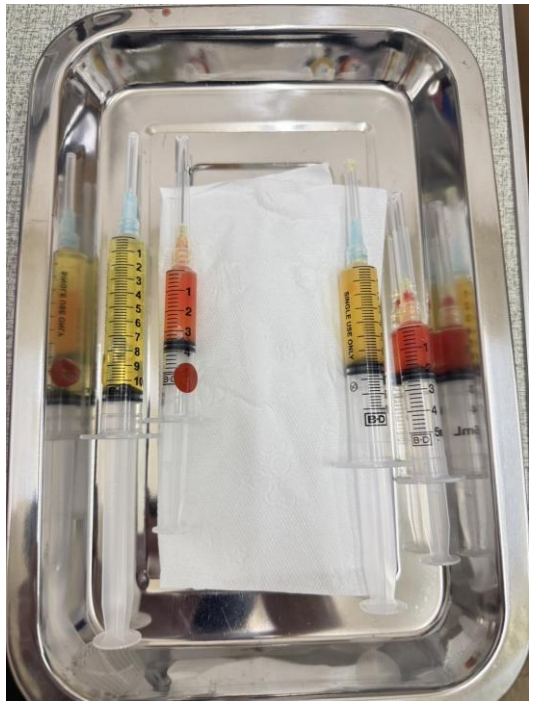


Vastly used in **surgeries** or **open cavities**, able to adhere and stay on wounds.

Eye Drops

Optimal for treating **Dry Eye Syndrome**, usage up to one month.

Injections

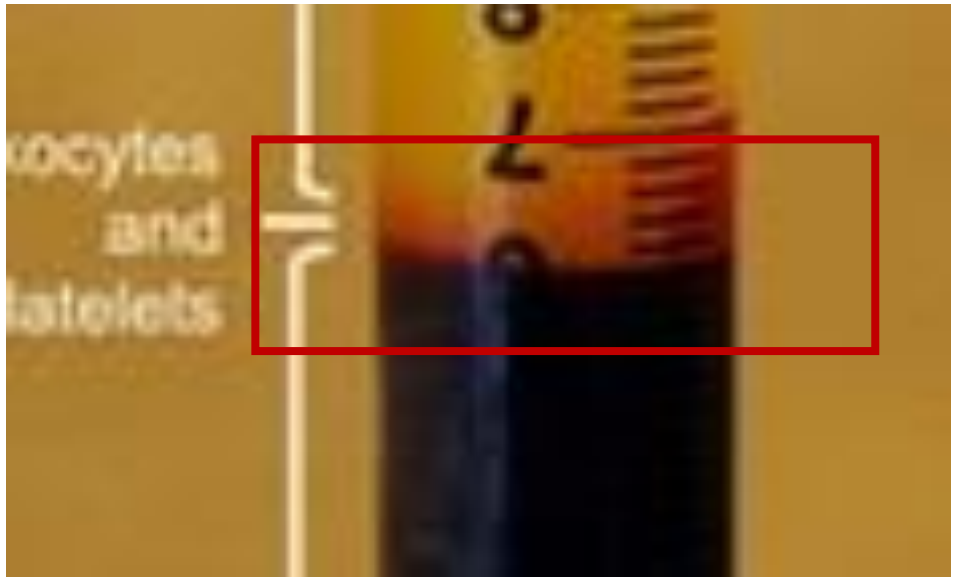


Spray

Suitable as **personalized skincare product**, brighten and rejuvenizing skin textures.

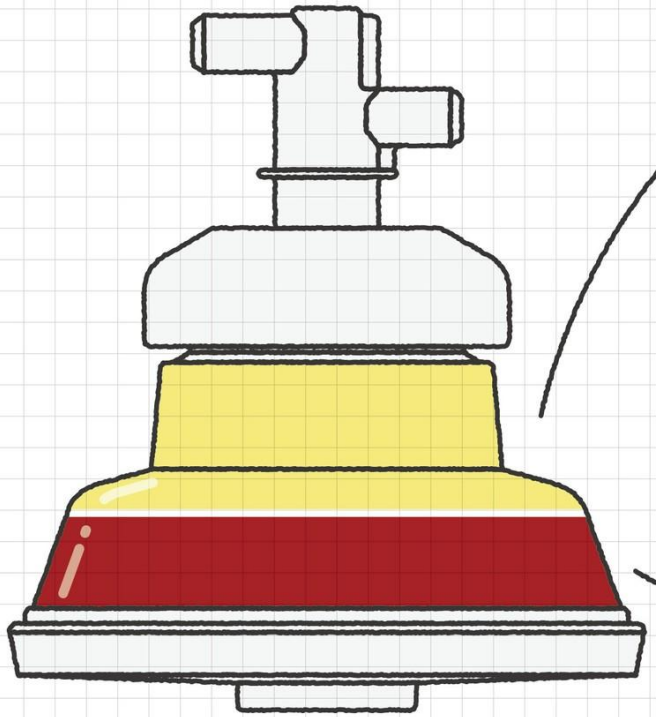
How to obtain BaM ?

High concentration of Bio-Active Molecules



Buffy coat

Blood Composition



55% PLASMA

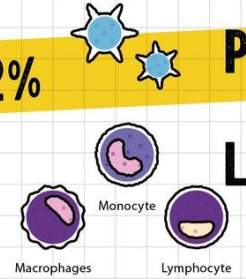
90% WATER

10% PROTEINS
ELECTROLYTES
METABOLIC NUTRIENTS
HORMONES

45% FORMED ELEMENTS

1-2% PLATELETS

LEUKOCYTES



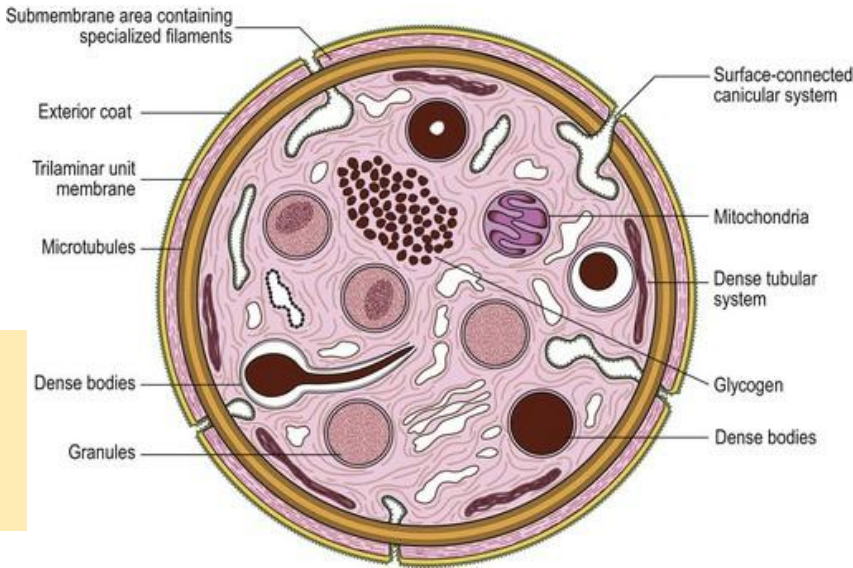
98-99% RED BLOOD CELLS

Platelets

–Precious and Sensitive Blood Components

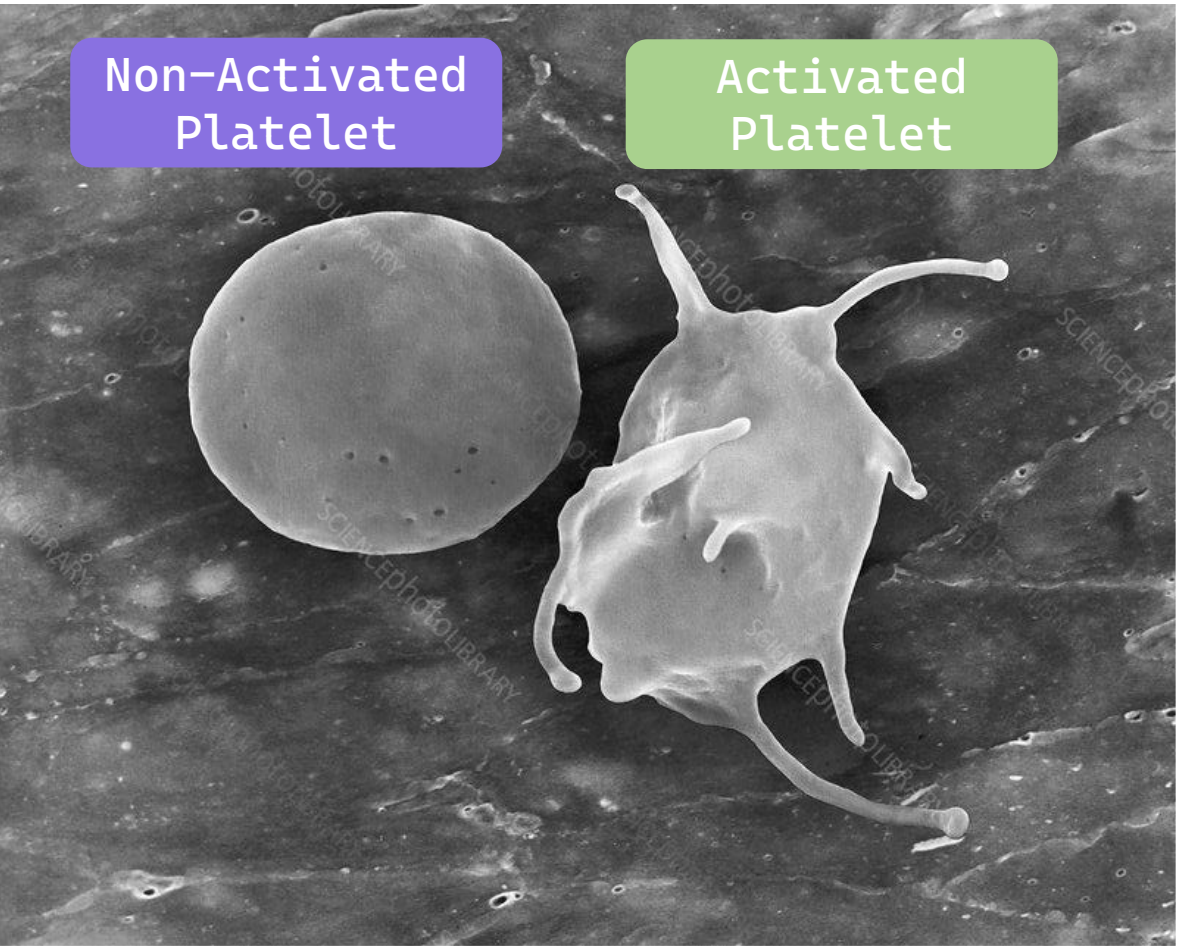
Easily degraded over time, platelets play a crucial role in tissue repair when damaged by trauma.

- Three-layered structure with multiple signaling receptors on the cell surface.
- Rich in signaling proteins and growth factors, along with cellular factors related to inflammation and regeneration, participating in the initiation and regulation of inflammatory cascades, leading to natural wound healing.
- **Platelets transmit information via their cellular receptors, relaying signals, activating repair mechanisms, and communicating with other cells to facilitate tissue healing.**
- Platelets constitute a small fraction of blood (<1%).
- Platelets undergo degradation due to lysis, triggered by trauma and time.



Capturing Platelets while maintaining its form is a great challenge!

Platelet protection is KEY



- Phoenix's Latham bowl design safeguards platelets, **preventing premature activation** and damage during centrifugation. Since platelets activate easily, improper handling can lead to suboptimal results.
- Preventing premature activation allows growth factors and resident macrophage to be precisely coordinated for each wound. **Engineered to minimize disruption from centrifugation, temperature, and handling**, it delivers high-quality BaM for superior results.

Impact of the Different Preparation Methods to Obtain Autologous Non-Activated Platelet-Rich Plasma (A-PRP) and Activated Platelet-Rich Plasma (AA-PRP) in Plastic Surgery: Wound Healing and Hair Regrowth Evaluation

Pietro Gentile,[1,*] Claudio Calabrese,[2] Barbara De Angelis,[1] Laura Dionisi,[3] Jacopo Pizzicannella,[4] Ashutosh Kothari,[5] Domenico De Fazio,[6] and Simone Garcovich[7]

Studies show that Non-Activated Platelets have significantly superior performances than activated platelets!

To better explain the different in vivo results obtained using A-PRP and AA-PRP, it appears necessary to report the most recent outcomes in hair density and hair count obtained for these treatments and to compare the results with Human Follicle Stem Cells injection. In detail, 12 weeks after the last injection (A-PRP and AA-PRP have been performed every 30 days, three times), hair density measurements for patients treated with A-PRP and AA-PRP were 65 ± 5 and 28 ± 4 hairs/cm^2 respectively. The results obtained constitute a $31 \pm 2\%$ increase in hair density when A-PRP treatment is performed versus $19\% \pm 3\%$ increase in hair density when AA-PRP treatment is performed, with a statistically significant difference in hair growth ($p = 0.0029$) [4]. Differences between the 12 weeks follow-up counts and the baseline count for these hair growth parameters were higher in the A-PRP treatment population than in the AA-PRP treatment population as reported in the previous trials performed by Gentile et al. [4]. Twenty-three weeks after the last injection, hair density measurements for patients treated with A-PRP and AA-PRP were 28 ± 2 and 15 ± 3 hairs/cm^2 respectively [4].

Non-Activated vs. Activated Platelets

Timing& Cell Quality Matters!

-Platelets finished releasing growth factors within one hour
→ **Processing time/Device is Crucial to BaM quality!**

Platelet-rich plasma (PRP): what is PRP and what is not PRP?

Marx RE. Implant Dent. 2001;10(4):225-8. doi: 10.1097/00008505-200110000-00002. PMID: 11813662.

APPLICATIONS OF PRP

PRP may be mixed into a bone graft, layered in as the graft is placed, sprayed on a soft tissue surface, applied on top of a graft, or used as a biologic membrane. However, clotting of the PRP should be done only at the time of use. Clotting activates platelets, which begin secreting their growth factors immediately (Fig. 2). Within 10 minutes they secrete 70% of their stored growth factors and close to 100% within the first hour (Fig. 3). They then synthesize additional amounts of growth factors for about 8 days until they are depleted and die. Therefore, clinicians should only clot (activate) PRP when they are ready to use it and not in advance. Clinicians should also critically assess publications, which may claim to advanced the concept of developing PRP from clotted blood or to companies that have promoted "serum separator tubes." Serum is not plasma and contains almost no platelets. It is impossible to develop PRP from clotted whole blood. Because the two functional roles of platelets in nature are initiation of healing and hemostasis, platelets become part of the physical blood clot and, therefore, the serum is devoid of platelets. PRP can only be developed from anticoagulated blood.

WHICH ANTICOAGULANT TO USE?

There are several choices of anticoagulants the clinician can use. However, only two support the metabolic needs of platelets and the viable separation of platelets in an undamaged manner. Anticoagulant citrate dextrose-A (ACD-A) is preferred

to those who may use a laboratory centrifuge to develop PRP or may purchase a device that is merely a modification of laboratory centrifuge. Such centrifuges are designed for diagnostic purposes—not PRP development. They may not produce a sufficient platelet yield, they may damage platelets, they may not use pyrogen free test tubes, and they are not FDA cleared. Therefore, they should not be used.

Clinical Usage

Application in Dermatology

Aesthetic& Rejuvenation

- Aesthetic& Rejuvenation: Wrinkle Reduction, Skin Firming & Lifting, Scar Repair
- Hair Implant
- Alopecia Areata
- Androgenetic Alopecia(AGA)
- Personalized Skincare

Wound Care

- Diabetes Wounds
- Burns& Scalds
- Skin grafting
- Decubitus ulcer
- Lichen Sclerosus of the Vulva

The Effect of Autologous Activated Platelet Rich Plasma (AA-PRP) Injection on Pattern Hair Loss: Clinical and Histomorphometric Evaluation

V. Cervelli,[1] S. Garcovich,[2] A. Bielli,[3] G. Cervelli,[4] B. C. Curcio,[1] M. G. Scioli,[3] A. Orlandi,[3] and **P. Gentile**[1,5]

Abstract

To investigate the safety and clinical efficacy of AA-PRP injections for pattern hair loss. AA-PRP, prepared from a small volume of blood, was injected on half of the selected patients' scalps with pattern hair loss. The other half was treated with placebo. Three treatments were given for each patient, with intervals of 1 month. The endpoints were hair re-growth, hair dystrophy as measured by dermoscopy, burning or itching sensation, and cell proliferation as measured by Ki-67 evaluation. At the end of the 3 cycles of treatment, the patients presented clinical improvement in the mean number of hairs, with a mean increase of 18.0 hairs in the target area, and a mean increase in total hair density of 27.7 (number of hairs/cm^2) compared with baseline values. Microscopic evaluation showed the increase of epidermis thickness and of the number of hair follicles two weeks after the last AA-PRP treatment compared to baseline value ($P < 0.05$). We also observed an increase of Ki67$^+$ keratinocytes of epidermis and of hair follicular bulge cells and a slight increase of small blood vessels around hair follicles in the treated skin compared to baseline ($P < 0.05$).

- Three-Month Treatment Protocol (Once Per Month)
- PRP Injection Dosage: 0.1 mL/cm²
- Targeted Effects: Increased hair volume and density
- Microscopic Observations:
  - Increased epidermal thickness
  - Follicle count increase two weeks post-treatment
  - Elevated Ki-67-positive keratinocytes in the epidermis
  - Increased microvascular density around hair follicles

Alopecia Areata

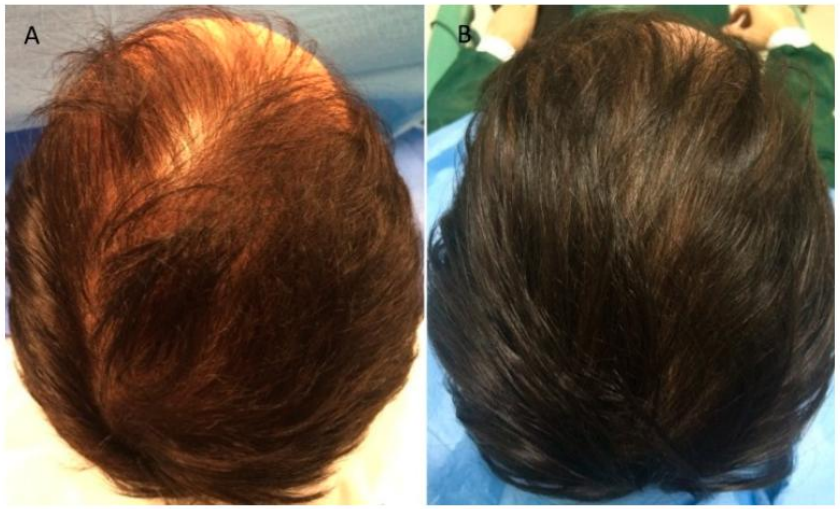
Androgenetic Alopecia

Injection Protocol:

- Dosage: 0.2 mL/cm²
- Depth: 5 mm
- Method: Mechanical injection using Ultim gun, 30G needle
- Frequency: Once every 30 days, for a total of three sessions
- Evaluation: Hair count measured using Trichoscan (per 0.65 cm²)

Evaluation of Not-Activated and Activated PRP in Hair Loss Treatment: Role of Growth Factor and Cytokine Concentrations Obtained by Different Collection Systems

For the A-PRP study, three treatments were administered over 30-day intervals. Trichoscan analysis of patients, three months post-treatment, showed a clinical improvement in the number of hairs in the target area (36 ± 3 hairs) and in total hair density (65 ± 5 hair cm^2), whereas negligible improvements in hair count (1.1 ± 1.4 hairs) and density (1.9 ± 10.2 hair cm^2) were seen in the region of the scalp that received placebo. Microscopic evaluation conducted two weeks after treatment showed also an increase in epidermal thickness, $Ki67^+$ keratinocytes, and in the number of follicles. The AA-PRP treatment groups received a singular



Results

- **Increased hair volume and density in the target area**
- **Thicker epidermis observed under a microscope**
- **Higher follicle count two weeks post-treatment**
- **Increased Ki-67-positive keratinocytes in the epidermis**
- **Greater number of hair follicles and surrounding microvasculature**

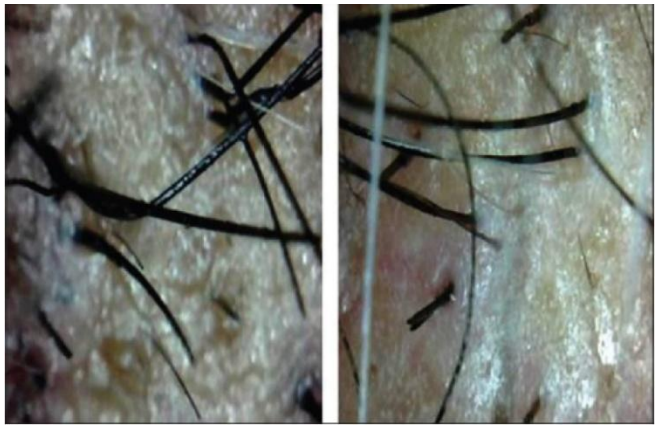
Hair Transplant

Outcome of Intra-operative Injected Platelet-rich Plasma Therapy During Follicular Unit Extraction Hair Transplant: A Prospective Randomised Study in Forty Patients

Suruchi Garg, J Cutan Aesthet Surg

In PRP group, all subjects had >75% hair regrowth at 6 months, density of >75% grafts was noticed in 12 patients at 4 weeks meaning reduced fall of transplanted hair during catagen phase. New hair growth started at 8 weeks in 16 patients and redness over recipient area completely disappeared in 19 patients at 3 months of surgery and activity in dormant follicles as fine thread like hair was noticed besides the thick transplanted hair in all subjects. In non-PRP group, four patients had >75% hair regrowth at 6 months; none showed >75% graft density at 4 weeks, and 13 subjects showed dormant follicle activity at 4 months. The number of patients having lengthier hairs was significantly more in PRP group.

New hair growth visible two months post-transplantation(under Microscopic Observation)

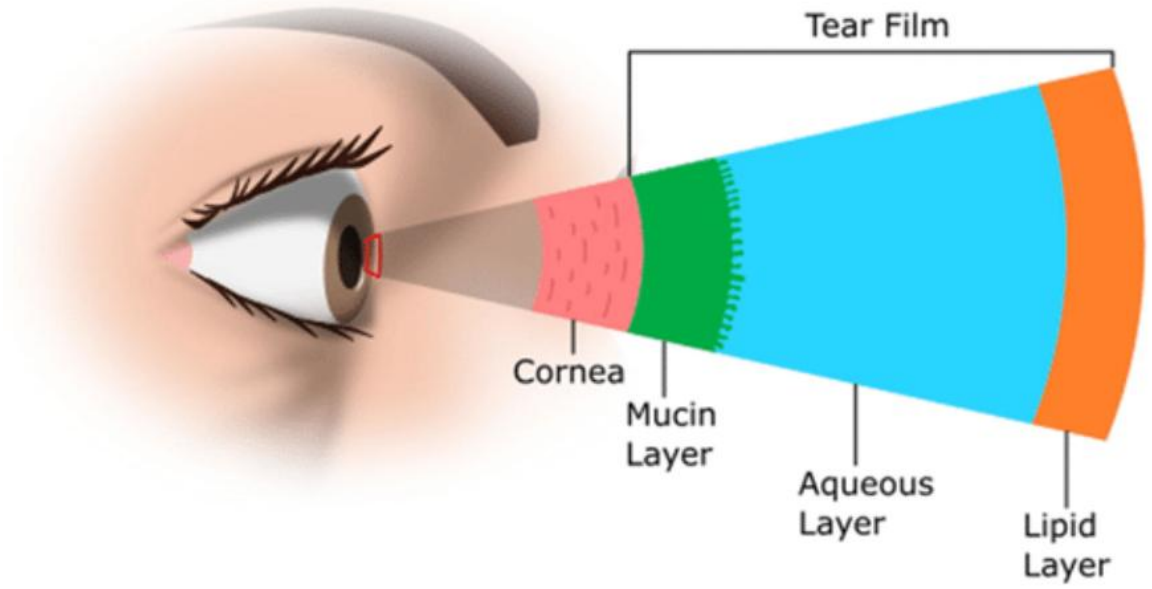


Reduced incidence of skin redness vs. control group

PRP Injections Benefit Hair Restoration by:

- Enhancing hair density
- Reducing catalytic loss of transplanted hair follicles
- Promoting skin repair
- Accelerating the growth of new hair after transplantation
- Reactivating dormant hair follicles

Application in Ophthalmology



Dry Eye Syndrome& Corneal Ulcer

Lipid Layer

Liquid at normal body temperature, prevents the evaporation of tears

Aqueous Layer

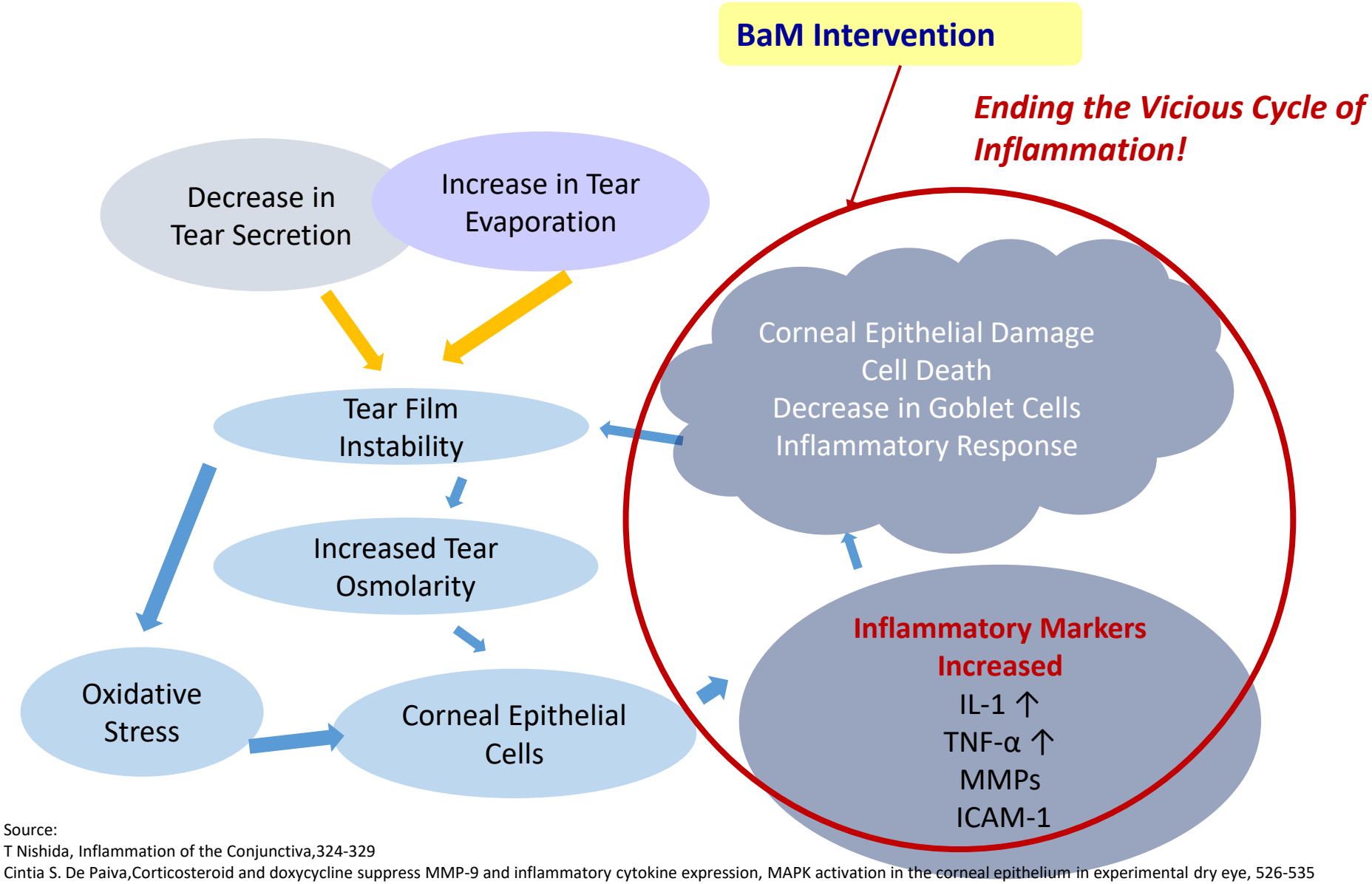
Composed of water, inorganic salts, organic compounds, **immunoglobulins**, and **lysozymes…**

Mucin Layer

A hydrophilic interface is formed between the corneal epithelial layer and the tear layer of the tear film, which serves **to nourish, protect the cornea and smooth the corneal surface**.

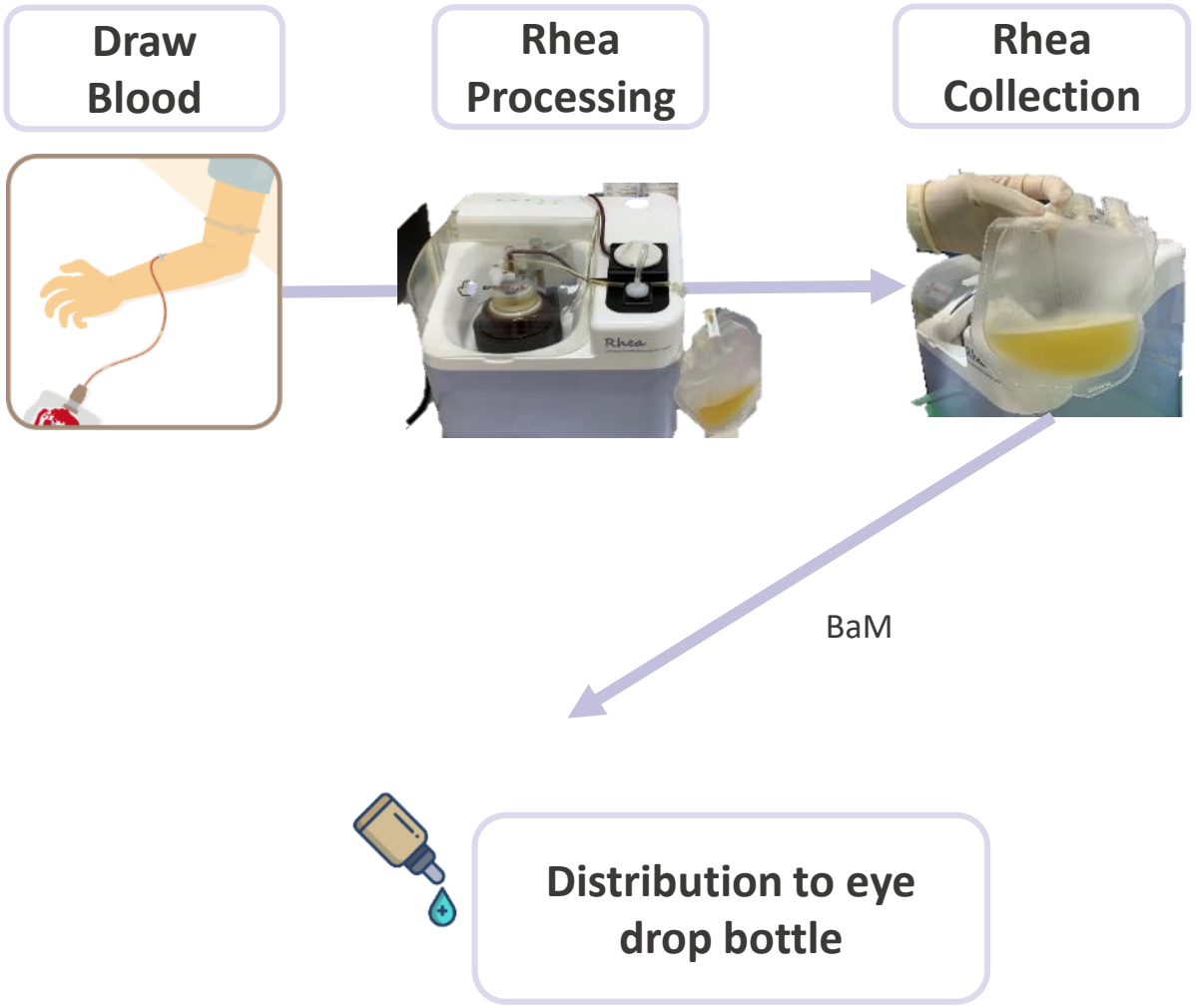
Damage to the tear film will lead to **increased inflammation** and **corneal damage**, creating a ***vicious cycle***

Mechanism of Dry Eye Syndrome



Source:
T Nishida, Inflammation of the Conjunctiva,324-329
Cintia S. De Paiva,Corticosteroid and doxycycline suppress MMP-9 and inflammatory cytokine expression, MAPK activation in the corneal epithelium in experimental dry eye, 526-535

BαM
For Dry Eyes



Features:

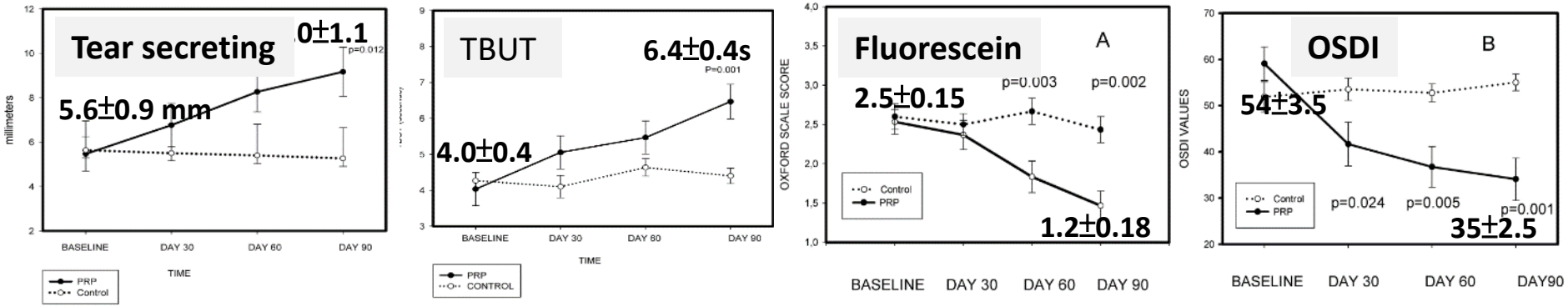
Harnesses the body's natural mechanisms to regulate platelet growth factor release, promoting epithelial cell repair and modulating inflammatory responses.
Stored in fridge and freezer, for one month of treatment

The Effect of Immunologically Safe Plasma Rich in Growth Factor Eye Drops in Patients with Sjogren Syndrome

Ronald Mauricio Sanchez-Avila et al. The Effect of Immunologically Safe Plasma Rich in Growth Factor Eye Drops in Patients with Sjogren Syndrome. *Journal of Ocular Pharmacology and Therapeutics.* Volume 33, Number 5, 2017

PRP Eyedrops/Injections prove to have significant improvement for Dry Eye syndromes!

Avila et al. (2018) conducted a controlled experiment on 30 patients with Sjögren's syndrome. Among them, 15 patients in the experimental group received a 1 ml PRP injection into the lacrimal gland, while the other 15 in the control group received a 1 ml hyaluronic acid injection. The results after 30 days, 60 days, and 90 days showed significant improvement in the PRP experimental group. This indicates that PRP injection is a safe and effective treatment method.



Solid line: PRP group； Dashed line: control group

Autologous PRP Eye Drops for the Treatment of Post-LASIK Chronic Ocular Surface Syndrome

80 patients who had undergone LASIK surgery, a total of 156 affected eyes were treated postoperatively with a single therapy of E-PRP applied 6 times daily for 6 weeks.

- Improvement in dry eye symptoms: 85%
- Improvement in keratitis: 89.6%
- Improvement in conjunctival hyperemia: 93.3%

TABLE 2: Signs and symptoms of post-LASIK ocular surface syndrome before and after monotherapy with autologous platelet-rich plasma eye drops.

	Number of cases before treatment *n* (%)	Worsening	No change	Improvement
Dry eye symptoms (patients)	80 (100%)	0 (0%)	12 (15%)	68 (85%)
Fluorescein staining (eyes)	116 (74.3%)	2 (1.7%)	10 (8.6%)	104 (89.6%)
Conjunctival hyperemia (eyes)	29 (18.7%)	0 (0%)	2 (6.7%)	27 (93.3%)

Jorge L. Alio . Autologous PRP Eye Drops for the Treatment of Post-LASIK Chronic Ocular Surface Syndrome

Autologous Platelet-Rich Plasma Eye Drops in the Treatment of Recurrent Corneal Erosions

Table 2. Treatment outcomes of patients and comparison between groups

	Conventional treatment group (n = 20)	PRP treatment group (n = 27)	*p*-value*
Follow-up (mon)	15.2 ± 17.4 (6-64)	14.6 ± 12.0 (6-42)	0.900
BCVA at final visit	0.84 ± 0.14	0.87 ± 0.14	0.400
Recurrences (total no. of episodes)			
Major	23	7	0.001
Minor	50	10	0.001
Mean frequency of recurrences	0.39 ± 0.24	0.06 ± 0.08	0.003

Values are presented as mean ± SD (range) or mean ± SD unless otherwise indicated.
PRP = platelet-rich plasma; BCVA, best-corrected visual acuity.
*Mann-Whitney *U*-test for difference between two serum groups.

Jun Jun Lee et al. Autologous Platelet-Rich Plasma Eye Drops in the Treatment of Recurrent Corneal Erosions. *Korean J Ophthalmol* 2016;30(2):101-107

Conclusion

1. A refined name for PRP: Bio-Active Molecule Therapy (BaM Therapy)

2. The core mechanism of BaM Therapy is driven by “signaling” and “macrophage mediation” .

3. Platelets act as the primary signaling initiators, releasing growth factors and essential signaling proteins.

4. BaM Therapy's effectiveness hinges on adequate platelet concentration.

5. Identifying platelets by the naked eye is impossible—automated digital sensors are the future of precision.