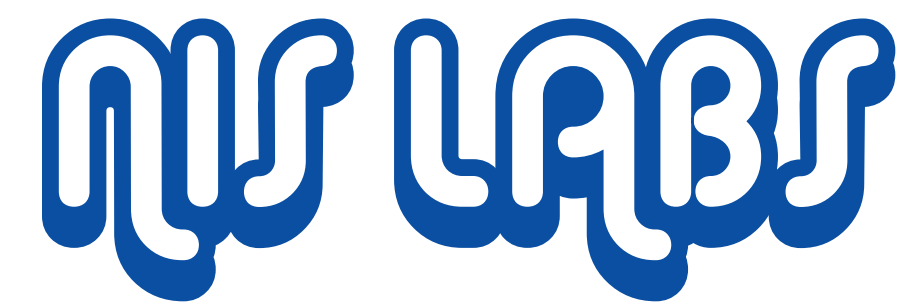


Effects of Ovacore™, a water-soluble egg membrane hydrolysate, on reduced inflammation, relief of joint pain, and support of skin health.



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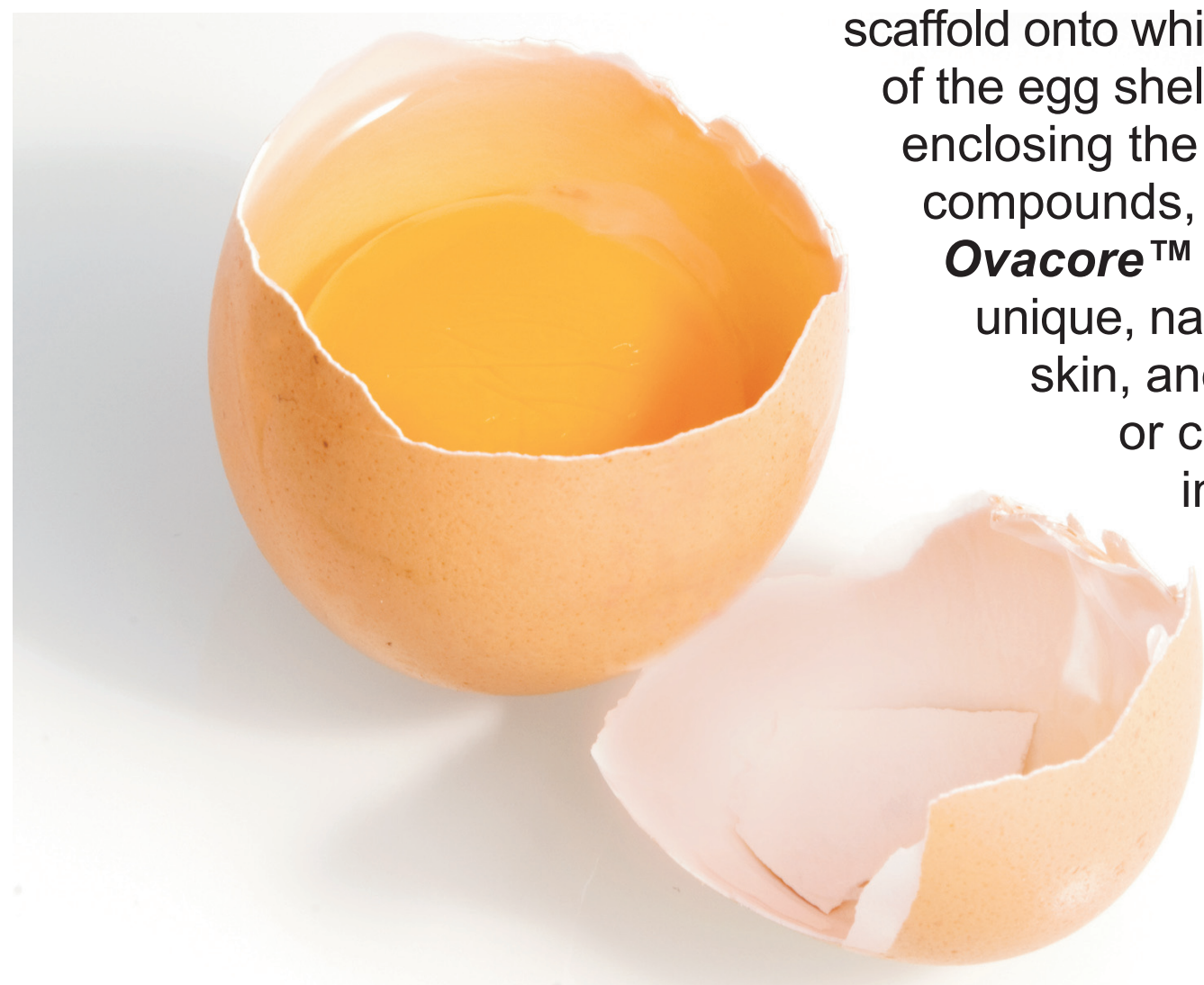
Ovacore™

Aim

The goal for this study was to evaluate anti-inflammatory and structural tissue support of joints, microvessels, and skin by the water-soluble, natural egg membrane hydrolysate Ovacore™.

Background

Nutritional products made from eggshells have been used historically as a source of calcium, and also for support of connective tissue, for example in joint health. Currently in the food industry, the commercial use of unfertilized eggs results in vast amounts of eggshells as a byproduct. **Eggshell** is the calcified matrix of glucosaminoglycans and other glycoproteins. Approximately 2-4% of the weight of egg shells is organic compounds; the rest of the weight is minerals, predominantly calcium. The organic compounds serve as a scaffold onto which the organized mineralization happens during the formation of the egg shell. **Egg membrane** is the thin membrane inside the egg shell, enclosing the egg white. This thin skin also has a matrix of organic compounds, however it has a distinctly different chemical composition. **Ovacore™** is manufactured from natural egg membrane to provide a unique, natural source of key bioactive compounds important for tissue, skin, and vascular structure and integrity. Ovacore™ is not enriched or concentrated, but provides the natural profile of compounds in egg membrane without contamination from egg shell. Ovacore™ is hydrolyzed to produce a water-soluble nutritional product that is useful as a functional ingredient in food, beverages, and nutraceutical formulations.



Bioactive compounds in Ovacore™

Active ingredients	Biological activity
Elastin	Joint, tissue, skin, and vascular elasticity
Desmosine/ Isodesmosine	Joint, tissue, skin, and vascular elasticity
Collagen	Support of joint and connective tissue health
Total glucosaminoglycans (GAG)	Support of joint and connective tissue health
Transforming growth factor-beta	Immune regulation, cellular proliferation/differentiation
Calcium*	None*
Antioxidants	ORAC 448µm TE/gram

Safety

- ✓ No adverse effects have been reported.
- ✓ No negative side effects or toxicity observed in blood chemistry analysis.
- ✓ No abnormal blood cell morphology.
- ✓ No significant increase in IgE antibodies towards egg allergens.

* The content of calcium in Ovacore™ is negligible, verifying minimal contamination of the product by components from the mineralized eggshell.

Ovacore™ mechanisms of action

Based on historical data from product use, knowledge of the ingredients, and data from cell-based in vitro work the following areas of biological activities are of clinical interest:

- Joint flexibility and health;
- Vascular elasticity and health;
- Skin elasticity and health.

In addition, Ovacore™ has anti-inflammatory activity. This is important in the light of the contribution of chronic inflammatory conditions to joint problems, skin problems, and declining cardiovascular health.

Thus, the biological activity of Ovacore™ reflects a synergy between support of tissue elasticity and strength and reduced inflammatory conditions.

Methods

The anti-inflammatory and tissue-supportive properties of Ovacore™ were evaluated in different experimental models:

1. Cellular assays in vitro;
2. Arthritic dogs;
3. Human pilot studies:
 - a. Joint functionality
 - b. Skin health

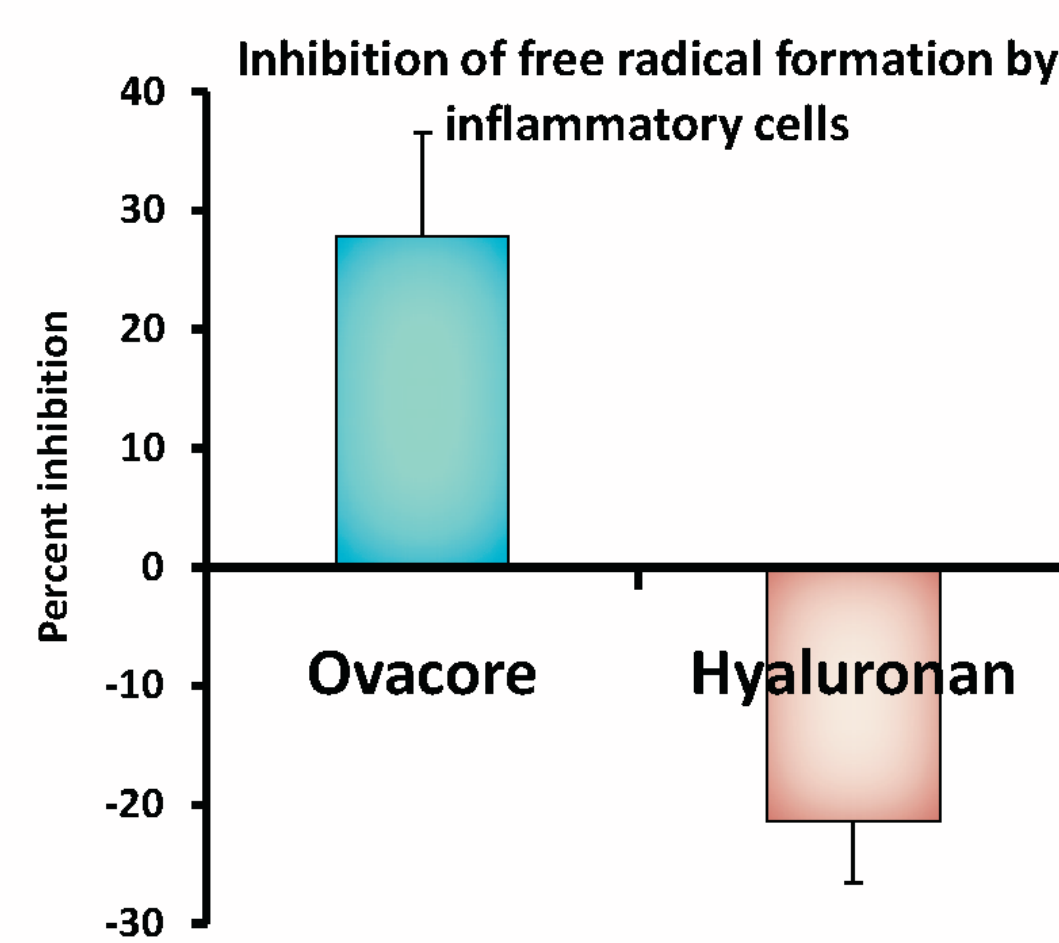


Cell-based and animal data

Anti-inflammatory properties of Ovacore™ in vitro:

The exposure of inflammatory cells to Ovacore™ in laboratory tests resulted in a reduced production of damaging free radicals. As a cellular model, polymorphonuclear cells from healthy human donors were used for the testing. Hydrogen peroxide (H₂O₂) was used to initiate an inflammatory response under oxidative stress conditions.

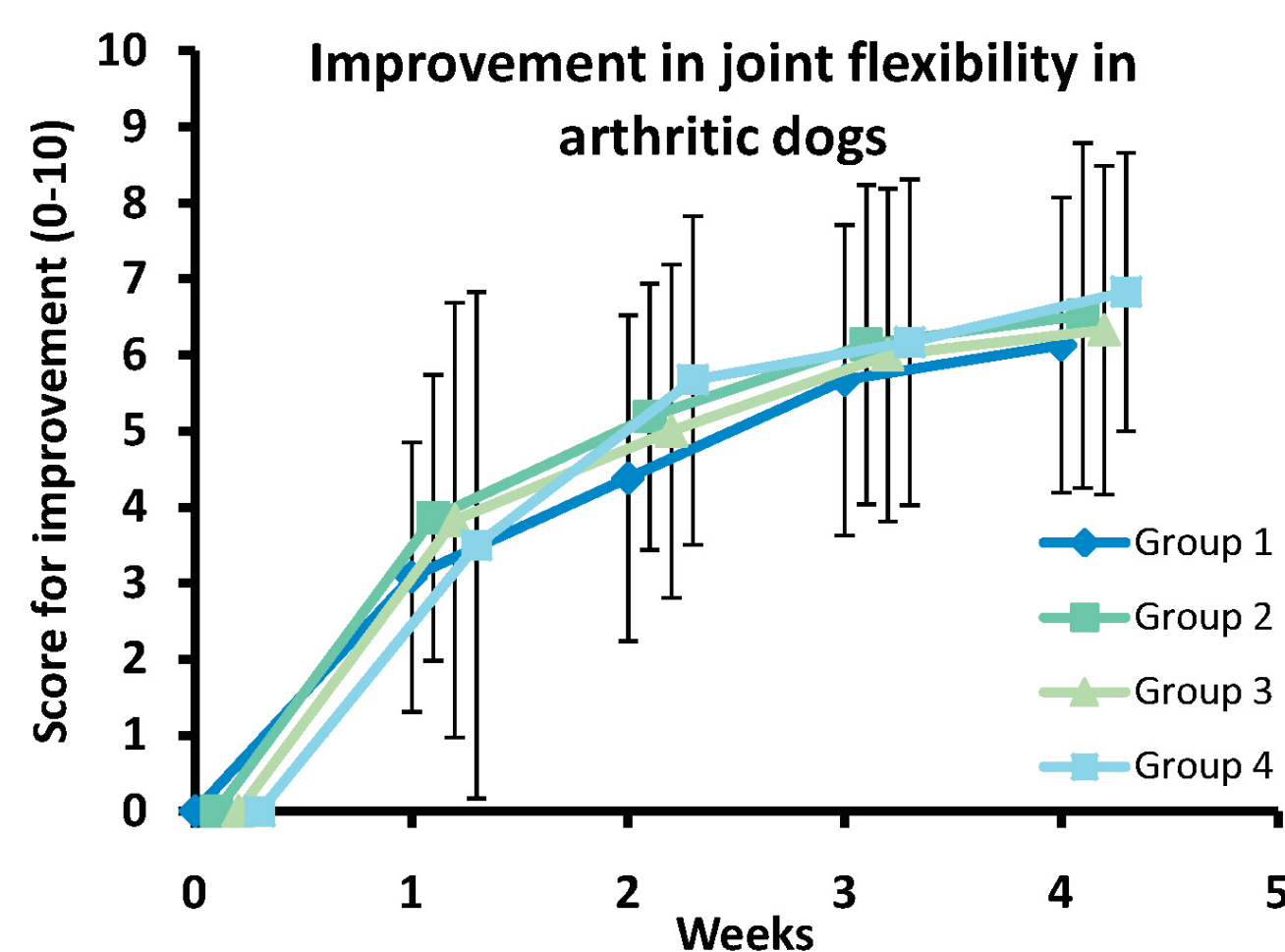
In parallel, a source of hyaluronan (75%) was tested in the assay. When the inflammatory cells were exposed to hyaluronan, the inflammatory cells responded in an opposite manner, and generated more free radicals in the assay. This is not surprising, due to the CD44 cell surface receptor for hyaluronan can transmit a pro-inflammatory signal in some cell types.



Arthritic dogs

Fifty-seven dogs with age-related arthritis and reduced mobility and activity levels were studied over a period of 28 days. The dose of Ovacore™ was 5 mg/pound body weight of the animal per day, given orally. No placebo group was included; i.e. all animals received Ovacore™. Sub-group analysis included analysis of improvements in relation to whether they had previously been given nutritional supplements for joint health. The average improvement was greater than 60% over the 4 weeks of study.

The improvements were statistically significant already after 1 week. In a subgroup of the dogs (n=27) that had previously taken a product containing omega-3 and glucosamine, the improvements were comparable to the improvements seen in dogs not previously on omega-3/glucosamine.



Human clinical data

Joint health study

An open-label pilot study was performed where 42 people with knee osteoarthritis were enrolled. Out of this population, 30 people completed the 6 week study.

Pain symptoms:

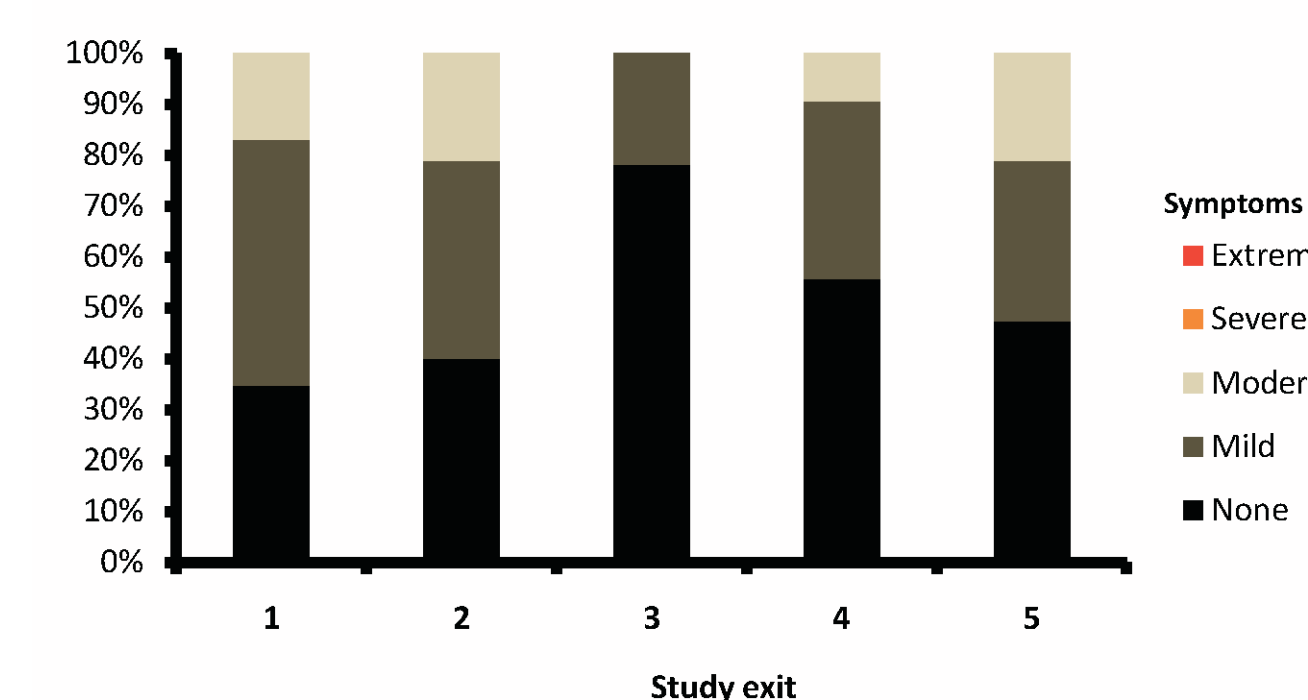
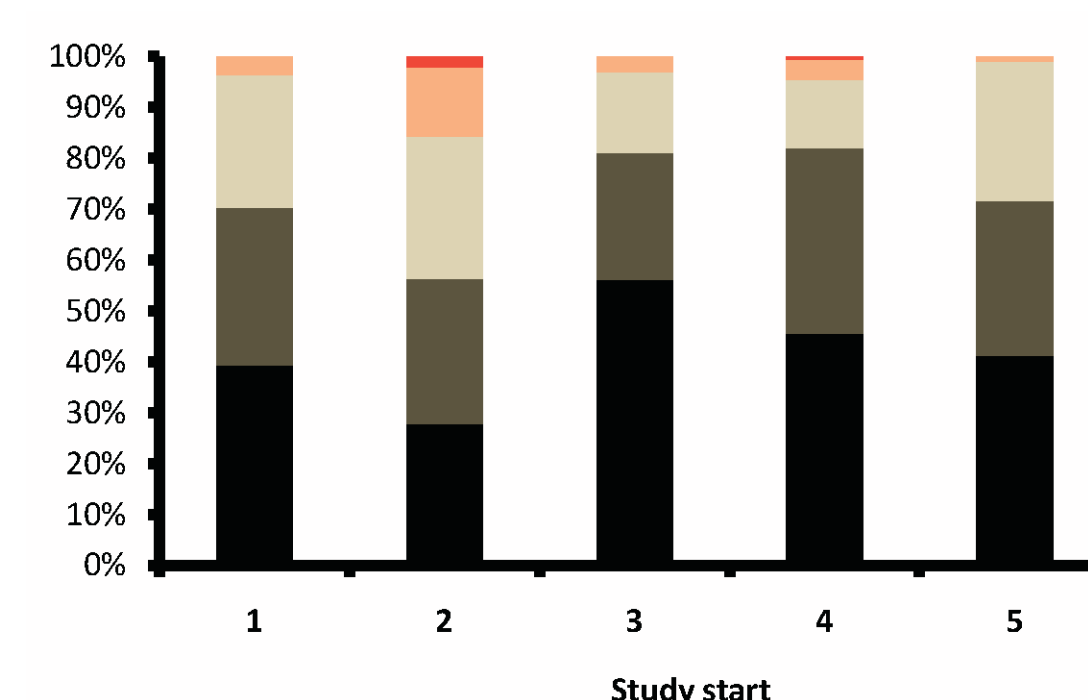
- Reduced 8.25% from baseline to 7 days
- Reduced 16.42% from baseline to 14 days.

WOMAC score:

- The WOMAC score showed >20% reduction from baseline to study end (p<0.0001).

Relative knee functionality:

- Joint function improved 37.8% over the course of the study.

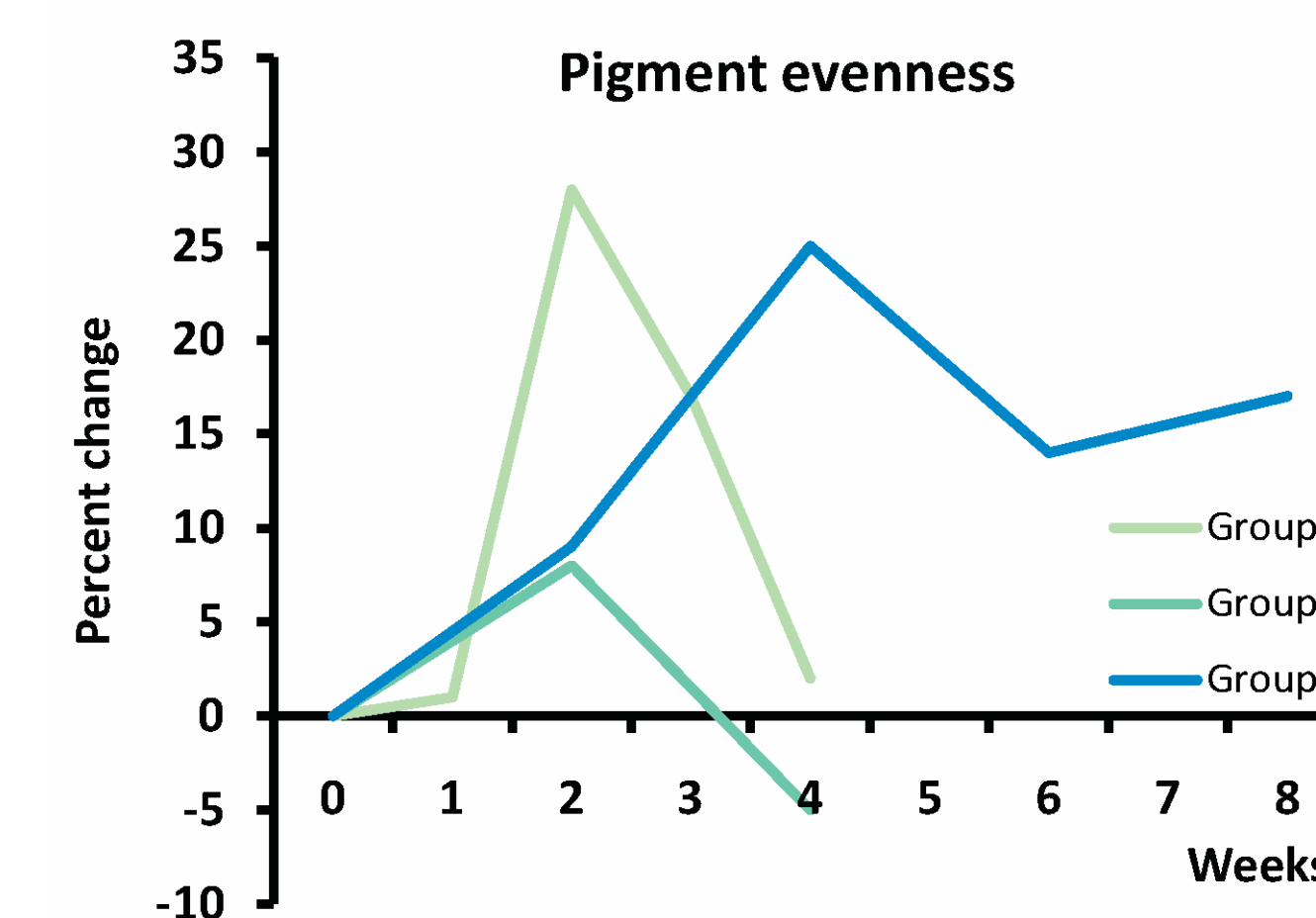
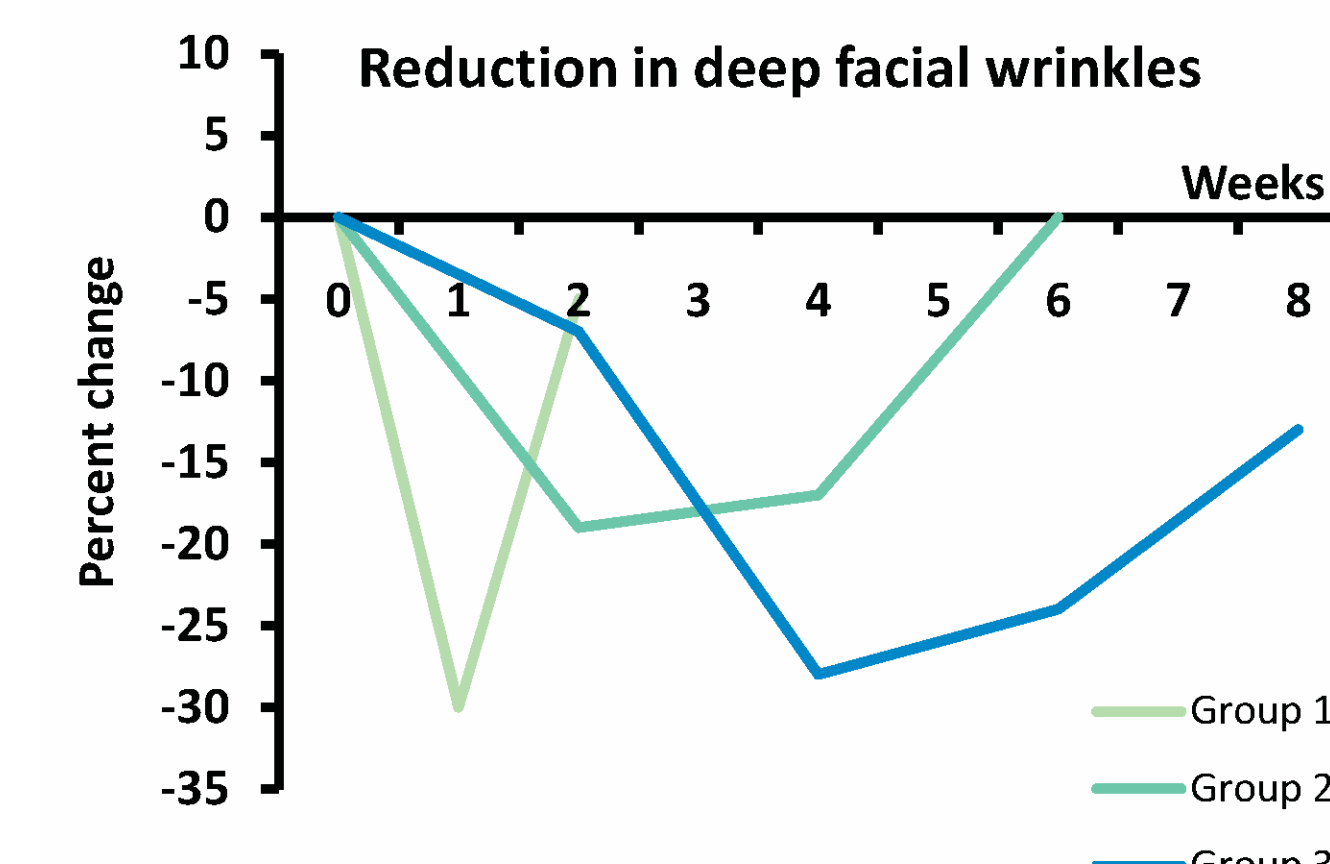


Skin health study

Twenty-three healthy adults with some degree of wrinkles, acne, and pore inflammation were recruited. The subjects were divided into three groups:

- Six (6) people applied product for 1 week;
- Nine (9) people applied product for 2 weeks;
- Eight (8) people applied product for 4 weeks.

Ovacore™ was applied to facial skin, and facial scans were performed using a Moritex/BTBP skin analyzer to quantify wrinkle severity and depth, skin complexion health, skin texture and laxity/tono, and UV damage. Study participants were followed for up to 4 weeks after product application had ceased. The score (number, severity, depth) of deep wrinkles was reduced in all three groups of study participants. Scores for skin complexion as an indicator of microvascular blood perfusion, showed improvements in all three groups.



The scores pertaining to excess sebum, acne, and pore inflammation were more variable. This is likely due to the small population size that could have led to uneven distribution of subjects with different types of skin problems at study start.

Further studies on skin inflammation, microvascular function, and pore health are warranted, and it is suggested that each study is targeted at well-defined types of skin problems.

Conclusion

Ovacore™ has anti-inflammatory and tissue-supportive biological activities, both after consumption and with topical use.

- Data from cell-based testing of mechanisms of action suggests strong anti-inflammatory activity of Ovacore™.
- This anti-inflammatory activity was confirmed in a study on arthritic dogs, where significant improvements were seen already at one week of adding Ovacore™ to their food.
- Furthermore, a study in humans has confirmed that joint flexibility and function improved with Ovacore™ consumption in people suffering from arthritis of the knee.
- Other aspects of reduction of inflammation were shown in humans suffering from acne and pore inflammation of the facial skin.
- In addition, support of skin elasticity and microvascular function was seen in the skin study by wrinkle reduction and improved healthy complexion of the skin.