

VARI® STAN PE – A Powerful Antibacterial Extract Derived from Garcinia Mangostana Fruit

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Introduction

Garcinia mangostana, commonly known as “mangosteen”, is a tropical evergreen tree. Its fruit is in an emerging category of novel functional foods sometimes called “superfruits” presumed to have a combination of appealing subjective characteristics, such as taste, fragrance and visual qualities, nutrient richness, antioxidant strength and potential impact for lowering risk of human diseases. The fruit of mangosteen is sweet, tangy, juicy and somewhat fibrous with an inedible, deep reddish purple-colored rind (pericarp) when ripe. Mangosteen is the plant mostly found in Asia, especially in Thailand. The pericarp of the mangosteen fruit is one of the richest sources of bioactive polyphenols, including xanthenes. With over 200 xanthenes identified in nature, so far 43 xanthenes have been identified in the mangosteen fruit which have remarkable biological activity. Therefore, the pericarp of this plant has been used as a medicinal drug in Southeast Asia for the treatment of skin infections, diarrhea, chronic wounds, heart therapy and inflammation. Conventional extraction methods are soxhlet or maceration processes. They operate at elevated temperatures and are time consuming. Other emerging extraction techniques use ultrasounds and seem to be more economical. In any case the quality of the extract from the pericarp is the key to achieve an effective activity. A high xanthone content, especially in alpha-mangostin, and the purity of the extract are important to guarantee a highly potent mangosteen extract.

The biological activities of xanthenes isolated from mangosteen include antioxidant, antitumoral, antibacterial, antiviral, antifungal, antiallergic and anti-inflammatory properties. In previous studies the antioxidant, anti-inflammatory and especially antibacterial properties of mangosteen extracts from its pericarp were investigated⁴⁻¹². Particularly the antibacterial activity against *Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus* (MRSA), *Staphylococcus epidermidis*, *Bacillus subtilis*, *Propionibacterium acnes*, *Pseudomonas aeruginosa*, *Salmonella enteritidis*, *Salmonella thyphimurium*, *Proteus* sp., *Klebsiella* sp., *Escherichia coli*, *Enterococcus* spp. and vancomycin resistant *Enterococci* (VRE) of the mangosteen has been demonstrated. Also the antityrosinase activity and antimicrobial power against the pathogenic bacteria in the oral cavity were successfully

reported⁴. Furthermore a chemopreventive action of mangosteen extracts was also investigated in the past¹⁻³.

For cosmetic applications, the antibacterial, antioxidant as well as anti-inflammatory effects of the mangosteen peel extract are of particular interest in deodorant and acne prone skin products. The antioxidant and anti-inflammatory features of the mangosteen peel extract are further interesting for products that protect from environmental aggressions such as UV light or generally improve the health of the skin. In the following investigations the mangosteen peel extract named Vari® Stan PE (patent pending) from Variati S.r.l. has been intensively investigated in order to show and proof its antibacterial and anti-inflammatory behaviors.

Minimum Inhibitory Concentrations of Vari® Stan (dry extract)

Vari® Stan PE consists of *Garcinia Mangostana* Peel Extract dissolved in natural propanediol. Its antibacterial properties have been previously assessed in vitro, evaluating the activity of the dry extract against a group of Gram+ strains, including *Staphylococcus aureus* and *Bacillus cereus*, bacteria present in many critical skin areas. The Minimum Inhibitory Concentration (MIC) values found (Table 1), confirm the strong and specific antimicrobial power of *Garcinia Mangostana* Peel Extract found in literature⁴⁻¹².

| Gram+ bacteria | MIC of dry extract [ppm] |
|-----------------------------------|--------------------------|
| <i>Staphylococcus aureus</i> | 1 |
| <i>Kocuria rhizophila</i> | 1 |
| <i>Staphylococcus epidermidis</i> | 1 |
| <i>Bacillus spizizenii</i> | 5 |
| <i>Bacillus cereus</i> | 10 |
| <i>Enterococcus hirae</i> | 1 - 5 |
| <i>Streptococcus pyogenes</i> | 1 |

Table 1: MIC values of *Garcinia Mangostana* Peel Extract

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Odor controlling properties of Vari® Stan PE tested in-vitro

In order to discover a possible deodorant power, a special in vitro test was conducted, using microbial strains isolated from armpit of human volunteers. The microorganisms were firstly identified, resulting principally Staphylococcus strains with a prevalent presence of Staph. epidermidis. Then, the activity of Vari® Stan PE was evaluated at different concentrations from 0.15% to 2.5% after 6 h and 18 h, respectively. The results in Figure 1 show a good antimicrobial efficacy already after 6 hours even at the lowest tested concentration of Vari® Stan PE (0.15%). Moving to 0.5% concentration, the antimicrobial activity is enhanced up to 18 hours, suggesting a long lasting effect can be expected for deodorant applications.

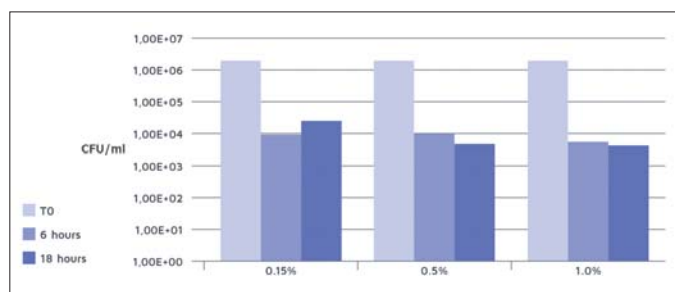


Figure 1: Antimicrobial efficacy of Vari® Stan PE against axillary microbial strains

Odor controlling properties of Vari® Stan PE tested in-vivo by sniff test

In order to define and position Vari® Stan PE as a good natural deodorant alternative, the product was evaluated in vivo by a sniff test. The aim of the study was evaluating Vari® Stan PE efficacy to counteract armpits odor formation in 10 volunteers (25 - 57 years old) affected by bromhidrosis (malodor sweating). The product efficacy has been evaluated 12 and 24 hours after a single application of a gel containing 1% Vari® Stan PE compared to a skin area treated with placebo, respectively. Score was set from 1 (no odor) to 5 (very strong odor). The odor evaluation was carried out, independently, by three well trained olfactory examiners. Data were reported in tables

| Ingredients | Placebo [%] | Product [%] |
|---|-------------|-------------|
| Aqua | qs | qs |
| Vari® Stan PE (Propanediol (and) Garcinia Mangostana Peel Extract | --- | 1.00 |
| PEG-40 Hydrogenated Castor Oil (and) PPG-26-Butheth-26 | 1.00 | 1.00 |
| Sodium Acrylate/Sodium Acryloyldimethyl Taurate Copolymer | 1.00 | 1.00 |
| Lactic Acid | 0.05 | 0.05 |
| Preservative | qs* | qs* |

*minimal sufficient quantity

Table 2. Formulations tested in sniff test

in their respective units and calculated by statistical analysis (Wilcoxon test). The tested formulations are given in Table 2. Figure 2 shows the data, expressed as mean values, obtained for both armpits treated with placebo or the active product. The study demonstrates a significant reduction of the armpit odor after 12 and 24 hours after the application of the gel with Vari® Stan PE compared to the skin area treated with placebo. The odor has been considered absent for the active product after 12 and 24 hours, confirming the long lasting deodorant features of Vari® Stan PE.

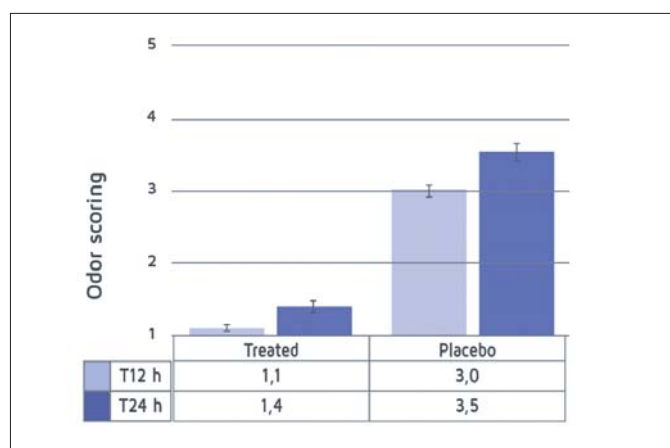


Figure 2: Odor scoring after 12h and 24h (test conducted on 10 volunteers)

At the end of the study, subjects were asked to reply to a self-assessment questionnaire in order to have an idea of the subjective perceived comfort using a deodorant product containing Vari® Stan PE. The questionnaire needed to investigate on the smell comfort after 12 and 24 hours from the product application; if any sweating reduction was also perceived; the soothing effect on skin irritation; and presence/absence of stains on clothes. All in all the product containing Vari® Stan PE resulted well tolerated by the subjects, also leaving a long lasting pleasant comfort.

Vari® Stan PE properties on acne prone skin

Propionibacterium acnes is a Gram+ resident bacteria of the skin's face follicles. It uses sebum as a nutrient for growth. People with acne tend to have more Propionibacterium acnes strains in their follicles than people without acne. Besides Propionibacterium acnes, other commonly resident bacteria (Staphylococcus epidermidis, Corynebacteria) are known to be involved in acneic skin disorders. Overall, stopping bacterial proliferation is one of the strategies needed for a successful cosmetic treatment of acneic skin. Following the above considerations and already knowing the strong antimicrobial properties of the pure dry extract, the product Vari® Stan PE was specifically tested against Propionibacterium acnes and Staphylococcus epidermidis. MIC and MMC (Minimum Microbicidal Concentration) are given in Table 3. The obtained values confirm the strong selective antimicrobial effect of Vari® Stan PE for cosmetic products addressed to acne prone skin subjects.

| Gram+ bacteria | MIC [%] | MMC [%] |
|----------------------------|---------|---------|
| Propionibacterium acnes | 0.005 | 1.0 |
| Staphylococcus epidermidis | 0.010 | 2.5 |

Table 3: MIC and MMC values of Vari® Stan PE against acne involved bacteria

In a clinical trial conducted on female volunteers with acne prone skin¹¹⁾ a significant decrease in acne lesions, including comedones, microcysts, papules and pustules after 28 days of treatment with a Garcinia Mangostana Extract was shown. This study, leading to a significant improvement of the skin appearance, confirms and fully advises the use of Garcinia Mangostana Extract for acne prone skin treatment.

Soothing effect of Vari® Stan PE – Clinical test on skin irradiated by a solar simulator

Mangosteen Extracts were reported¹³⁾ to strongly inhibit the prostaglandin E2 release (Figure 3). Particularly, α -mangostin inhibits COX-1 and COX-2 activities in vitro, suggesting a beneficial use for anti-inflammation treatments. On that base, the evaluation of the soothing effect of Vari® Stan PE was carried out on 20 volunteers with phototype I, II, III, inducing skin erythema by UVA/UVB irradiation. Vari® Stan PE was tested in a cream at 0.5% (Sample A) and 1% (Sample B), respectively. Measurements were carried out after UV irradiation and 30 minutes, 1, 2, 4, 24 hours after the application of the products, respectively. Area treated with placebo and untreated area (no product applied) were also evaluated for comparison. A significant decrease in erythema index was observed

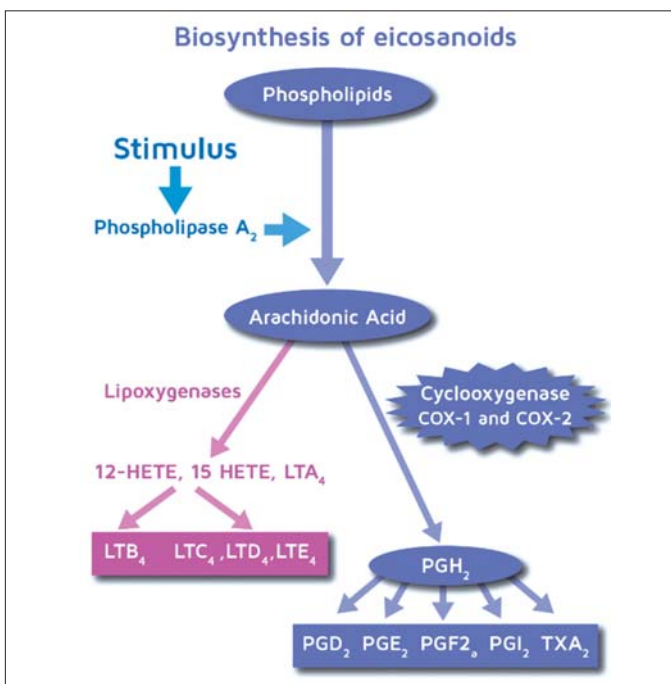


Figure 3: Biosynthesis of eicosanoids involved in inflammation process

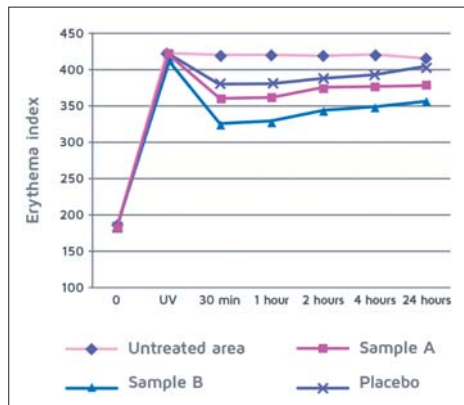


Figure 4: Mean values of the erythema index obtained at different times after irradiation and after sample application

already after 30 minutes from the treatment with Vari® Stan PE at both concentrations (Figure 4). Digital pictures also show an evident reduction of the redness between the area irradiated by a UVA/UVB and the same area after 30 minutes from the application of the cream containing Vari® Stan PE at 0.5% (Sample A) (Figure 5). Results from in vitro/in vivo show no evidence of adverse effects.



Figure 5: Soothing effect of Vari® Stan PE (0.5%): skin after UVA/UVB irradiation (Tuv) compared to 30 minutes after product application (T30 min)

Applications

Vari® Stan PE gives the cosmetic products an antibacterial and soothing action. It can be easily incorporated into all kinds of formulations. Various types of formulations and product forms are possible, such as

- Deodorants
- Acne prone skin products (gel, cream)
- After shave products
- After sun products
- After depilatory products
- Day care products

Conclusion

Due to its demonstrated efficacy against Gram+ bacteria as well as the strong odor control benefits, Vari® Stan PE can be considered an effective natural alternative in deodorant applications. Vari® Stan PE

is also suggested for the treatment of acne and inflammation prone skin thanks to its proved antibacterial and anti-inflammatory behavior. The soothing action, demonstrated by the UV irradiation test also justifies the use of Vari® Stan PE in after shave, after depilatory and after sun cosmetic products as well as in general skin, hair and personal care cosmetic products. The natural origin of both extract and solvent makes Vari® Stan PE suitable for natural derived cosmetics. Suggested dosage range of Vari® Stan PE is 0.5 - 1%. It is stable in a wide pH range 4-7. The emollient, humectant and feel properties of the solvent propanediol provide additional performance benefits, such as an excellent sensorial profile.

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