Microsilver BG™

Microsilver BG™ has revolutionised skin care, wound care and animal care worldwide.

It is a unique, patented ingredient which is produced through a physical process using highly-refined medical grade pure silver (99.99%). It is a pure elemental dry silver powder consisting of highly porous & micro-sized particles of pure silver, that provides a continuous and lasting generation of silver ions over time even in complex environments (sweat, blood, wound drainage fluid, urine). Its antimicrobial action on the surface of the skin is provided against unwanted germs but without harming the resident skin flora (good resident bacteria). It is a natural ingredient, NPA (USA) – ECOCERT / COSMOS (EU) certified for use in natural cosmetic products. It has been used in cosmetics, skincare, oral & personal care, wound care, bone cement, dental fillers. Average particle size is 10μm and the absence of nanoparticles is certified, which assures high product safety as micro-particles do not penetrate skin or mucosa tissue.

Gram + and Gram – bacteria are killed by silver ions Ag+ that are released from the particle depot. Unique porous structure provides efficient silver ion generation at low usage levels and helps particles cling to the surface of the skin. Particles remain on the surface of the skin (as confirmed by independent studies[1]) and help inhibit bacteria and fungus growth and promote skin's healing process. The antimicrobial action has the mechanism below:

- Microsilver BG™ on contact with the skin surface generates positive ions (Ag+) that are able to physically interact with the cell structure of various pathogenic bacteria. The positively charged silver ions attach to many negatively charged components of the pathogen including the trans-membrane proteins, the intracellular enzymes, ribosomes and nucleic acids.
- This binding action results in the damage to cell membranes leading to structural changes, including increased permeability, ultimately resulting in bacterial cell death.
- The silver ions also bind to the negatively charged nucleic acids in the DNA, leading to disruption of DNA replication and cell death.
- Silver ions interact with a number of intercellular enzymes leading to arrest of bacterial cell metabolism. Alterations in protein synthesis further weaken the survivability of the bacteria and contribute to the destabilization of the composition of the outer membrane. The membrane damage further induces the release of reactive oxygen species (ROS), forming free radicals with a powerful bactericidal action against transient pathogens.

Microsilver BG™ also has anti-biofilm action. *Staphylococcus pseudintermedius* and *Pseudomonas aeruginosa* are known biofilm producers, a recognized virulence factor in canine bacterial infections. In vitro studies have shown that Microsilver BG™ at various concentrations and a Microsilver BG™ containing topical product effectively inhibit biofilm formation of both Pseudomonas and Staphylococcal bacteria[2-3].

Grapefruit (*Citrus paradisi*) seed extract

Grapefruit Seed Extract (GSE) is a commercial product derived from the seeds and pulp of grapefruit (*Citrus paradisi* Macf., Rutaceae). Chemical research revealed the presence of flavonoids, ascorbic acid, tocopherols, citric acid, limonoids, sterols and minerals in

grapefruit seeds and pulp. Its extend and level of antimicrobial effects was established in an array of studies.

Ethanolic extract exhibited the strongest antimicrobial effect against *Salmonella enteritidis* (MIC 2.06%, m/V)[4]. In another study[5] patchouli, tea tree, geranium, lavender essential oils and grapefruit seed extract were used singly and in combination to assess their anti-bacterial activity against three strains of Staphylococcus aureus: Oxford *S. aureus* NCTC 6571 (Oxford strain), Epidemic methicillin-resistant *S. aureus* (EMRSA 15) and MRSA (untypable). A combination of GSE and geranium oil showed the greatest-antibacterial effects against MRSA, whilst a combination of geranium and tea tree oil was most active against the methicillin-sensitive *S. aureus*.

The anti-biofilm effect of GSE was investigated against biofilm-forming strains of Staphylococcus aureus and Escherichia coli[6]. The GSE minimum inhibitory concentration (MIC) for *S. aureus* and *E. coli* were 25 µg/ml and 250 µg/ml, respectively. To investigate biofilm inhibition and degradation effect, crystal violet assay and stainless steel were used. Biofilm formation rates of four strains (*S. aureus* 7, *S. aureus* 8, *E. coli* ATCC 25922, and *E. coli* O157:H4 FRIK 125) were 55.8%, 70.2%, 55.4%, and 20.6% at 1/2 × MIC of GSE, respectively. The degradation effect of GSE on biofilms attached to stainless steel coupons was observed (≥ 1 log CFU/coupon) after exposure to concentrations above the MIC for all strains and ½ × MIC for *S. aureus* 7. Therefore, GSE might be used as an anti-biofilm agent that is effective against *S. aureus* and *E. coli*.

In a recent study[7], the inhibitory activities of grapefruit seed extract (GSE) on avian influenza virus (AIV), Newcastle disease virus (NDV), infectious bursal disease virus (IBDV), *Salmonella Infantis* (SI) and *Escherichia coli* (EC) were evaluated. GSE showed virucidal activity against AIV and NDV, namely enveloped viruses, but was not able to show virucidal activity against non-enveloped virus—IBDV. GSE showed high efficacy against bacteria such that the bacterial count of GSE×1,000 was undetectable in 0% FBS condition after 5 sec. In 5% FBS condition, GSE×1,000 was able to reduce the bacterial count to an acceptable level (RF>3) in 5 sec. The high bactericidal activity of GSE is possibly mediated by its ability to destroy the cytoplasmic membrane of bacteria[8]. In the present study, only gram negative bacteria were used.

Candida albicans (C. albicans), which is frequently isolated from denture plaque, is the main microorganism involved in the pathogenesis of denture stomatitis (DS). As *C. albicans* has a high affinity to acrylic resin denture-base material, it adheres easily to and forms a dense biofilm on denture surfaces. The cleansing effect of GSE on C. albicans biofilms formed on denture-base resin and the effects of GSE on the mechanical and surface characteristics of the resin were investigated[9]. Among the cleansing solution groups, 1% GSE almost completely diminished the biofilm formed on disc surfaces compared with 0.1% GSE, Polident, and 0.1% G+P, among which no significant differences were noted. The data also suggested that immersion in the solution containing GSE does not cause surface deterioration of denture-base resin.

REFERENCES

1. http://www.scc-quebec.org/wp-content/uploads/2018/11/Microsilver-181005_Montreal_MicroSilver.pdf

2. Bio-Gate, Studies on file
3. https://www.vetbiotek.com/research-studies
4. Z Cvetnić and S. Vladimir-Knezević: Antimicrobial activity of grapefruit seed and pulp ethanolic extract, Acta Pharm. 54 (2004) 243– 250
5. Edwards-Jones, R. Buck, S.G. Shawcross, M.M. Dawson, K. Dunn. The effect of essential oils on methicillin-resistant *Staphylococcus aureus* using a dressing model. *Burns* 30 (2004) 772–777
6. Ye Ji Song, Hwan Hee Yu, Yeon Jin Kim, Na-Kyoung Lee, and Hyun-Dong Paik Anti-Biofilm Activity of Grapefruit Seed Extract against *Staphylococcus aureus* and *Escherichia coli J. Microbiol. Biotechnol*. (2019), 29(8), 1177–1183
7. Miyuki Komura, Mayuko Suzuki, Natthanan Sangsriratanakul, Mariko Ito, Satoru Takahashi, Md. Shahin Alam, Mizuki Ono, Chisato Daio, Dany Shoham And Kazuaki Takehara Inhibitory effect of grapefruit seed extract (GSE) on avian pathogens *Vet. Med. Sci.* 81(3): 466–472, 2019
8. Heggers, J. P., Cottingham, J., Gusman, J., Reagor, L., McCoy, L., Carino, E., Cox, R. and Zhao, J. G. 2002. The effectiveness of processed grapefruit-seed extract as an antibacterial agent: II. Mechanism of action and in vitro toxicity. *Altern. Complement. Med*. 8: 333–340
9. Chiaki Tsutsumi-Arai, Kensuke Takakusaki, Yuki Arai, Chika Terada-Ito, Yusuke Takebe, Takahiro Imamura, Shinji Ide, Seiko Tatehara, Reiko Tokuyama Toda, Noriyuki Wakabayashi, Kazuhito Satomura Grapefruit seed extract effectively inhibits the *Candida albicans* biofilms development on polymethyl methacrylate denture-base resin. PLOS ONE | https://doi.org/10.1371/journal.pone.0217496