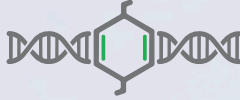


BioMedical EMPORIUM



BioMedical Emporium **ANTI-ACNE SERUM**

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COSMECEUTICAL SIGNIFICANCE

Acne vulgaris, commonly referred to as acne, is a chronic immune-inflammatory disorder of the pilosebaceous unit. It is clinically characterized by comedones, papules, pustules, nodules, or cysts. It can often cause sequelae such as scarring and dyschromia. The disorder affects up to 85 % of adolescents and young adults but sometimes remains a significant problem into adulthood especially in women. More than 40 % of women are affected by acne after the age of 25. The pathophysiology of acne involves abnormal follicular keratinization, sebum production, inflammation, and *Cutibacterium acnes* activity.

The critical role of inflammation in the pathogenesis of acne, from the formation of microcomedones to the development of secondary lesions such as scars and post-inflammatory hyperpigmentation, is gaining increasing scientific attention. While acne can resolve with appropriate treatment there remains a risk of permanent scarring particularly if treatment is delayed. Thus, it is imperative to consider a topical combination therapy suitable for daily use that addresses the inflammatory components of acne, prevents secondary infections, and promotes the healing of both inflammatory and non-inflammatory lesions.

The BioMedical Emporium Anti-Acne Serum is scientifically formulated to clinically aid in the treatment of acne-prone skin. BioMedical Emporium Anti-Acne Serum includes a gentle yet powerful combination of cosmeceutical ingredients to facilitate skin calming, decrease sebum production, and improve dermal aesthetic appearance.

The formulation includes several dermal bioactive ingredients, some of which are discussed below, starting with retinol. The main modes of action associated with topical retinoids like retinol are keratolytic and comedolytic by improving cell differentiation and increasing follicular epithelial turnover. Topical retinoids are regarded safe and efficacious for the treatment of acne vulgaris and can be used in combination with other bioactive ingredients to optimize results.

Topical niacinamide, an active form of vitamin B3, is beneficial in the treatment of acne vulgaris due to its sebum-suppressive, anti-inflammatory, and healing properties. Niacinamide is also recognized for its significant dermal benefits including the protection of the skin barrier.

The inclusion of topical salicylic acid, also known as a keratolytic agent, exhibit comedolytic properties and promote dermal cellular turnover. Additionally, salicylic acid's lipophilic nature facilitates its permeation into the sebaceous glands thereby aiding in the regulation of sebum production.

Lastly, tea tree oil, which is highly bioactive, is included as an effective bactericidal, fungicide, and antiseptic agent. Tea tree oil is obtained by steam distillation of the leaves and twigs of the native Australian tree *Melaleuca alternifolia* (Maiden & Betche) of the Myrtaceae family. The oil contains about 100 components present in various concentrations, among which the following predominate: terpenen-4-ol, γ -terpinene, α -pinene, and α -terpinene. In addition, it exhibits antioxidant, anti-inflammatory, and analgesic activity. The lipophilic components of the oil can also accelerate permeation into the cells of microorganisms, inhibiting metabolism, and facilitating subsequent death. In addition, it offers advantages over antibiotics since tea tree oil is less susceptible to developing antimicrobial resistance.

THE CLINICAL POTENTIAL OF RETINOL

Skin calming agent

Cosmeceutical features:

↓ redness, ↓ swelling, ↓ acne flare-ups

Physiology: ↓ TLRs, ↓ leukocyte migration, ↓ AP-1 pathway, ↓ inflammatory cytokines, ↓ nitric oxide, ↓ cellular inflammation, ↓ oxygen free radicals, ↑ RARs, ↑ RXRs

Combined anti-inflammatory and antimicrobial action

Cosmeceutical features:

↓ redness, ↓ swelling, ↓ infection of acne-affected skin, ↑ dermal healing

Physiology: ↓ lipoxygenase pathways, ↓ TLRs, ↓ AP-1 formation, ↓ normalize hyperkeratinization, ↓ hypercornification of the pilosebaceous unit, ↑ aerobic environment, ↓ oxygen free radicals, ↑ RARs, ↑ RXRs

Decreases sebum production

Cosmeceutical features:

↓ oily skin appearance, ↓ acne flare-ups

Physiology: ↓ lipid synthesis of sebocytes

Reduces pore size

Cosmeceutical features:

↑ appearance of primary acne lesions, ↑ appearance of secondary acne lesions, ↓ pigmentation intensity, ↓ comedones

Physiology: ↑ epidermal turnover, ↓ normalize hyperkeratinization, ↓ hypercornification of the pilosebaceous unit

THE CLINICAL POTENTIAL OF SALICYLIC ACID

Skin calming agent

Cosmeceutical features:

↓ redness, ↓ swelling, ↓ acne flare-ups

Physiology: ↓ inflammation, ↓ NF-κB, ↓ AMPK/ SREBP-1 pathway, ↓ COX-2 expression, ↓ IL-1β, ↓ IL-6, ↓ TNF-α

Combined anti-inflammatory and antimicrobial action

Cosmeceutical features:

↓ redness, ↓ swelling, ↓ infection of acne-affected skin, ↑ dermal healing

Physiology: ↓ NF-κB, ↓ AMPK/ SREBP-1 pathway, ↓ FAS, ↓ ACC, ↓ COX-2 expression, ↓ IL-1β, ↓ IL-6, ↓ TNF-α

Decreases sebum production

Cosmeceutical features:

↓ oily skin appearance, ↓ acne flare-ups

Physiology: ↓ sebocyte lipogenesis, ↓ SREBP-1a, ↓ SREBP-1c

Reduces pore size

Cosmeceutical features:

↑ appearance of acne scars, ↑ unclogging of pores, ↑ dermal healing

Physiology: ↑ cell turnover, ↓ OSM, ↓ STAT3, ↑ dissolving of desmosomes

THE CLINICAL POTENTIAL OF NIACINAMIDE

Skin calming agent

Cosmeceutical features:

↓ redness, ↓ swelling, ↓ acne flare-ups

Physiology: ↑ mast cell stabilization, ↓ inflammatory cytokine synthesis, ↑ NAD⁺, ↑ fibroblast senescence, ↑ normal fibroblast activity maintenance

Combined anti-inflammatory and antimicrobial action

Cosmeceutical features:

↓ redness, ↓ swelling, ↓ infection of acne-affected skin, ↑ dermal healing

Physiology: ↓ ROS, ↓ SIRT, ↑ PARP-1, ↓ COX-2, ↑ BCL6 expression, ↓ PGE2, ↓ NOS, ↓ TNF-α, ↓ IL-1, ↓ IL-6, ↓ IL-8, NF-κB, ↑ IL-10, ↑ MRC-1, ↓ MHC class II, ↓ interferon-γ, ↓ SASP, ↓ mast cell degranulation in dermis, ↑ cellular equilibrium, ↓ biofilm formation, ↑ AMP, ↑ LL-37 bioavailability

Decreases sebum production

Cosmeceutical features:

↓ oily skin appearance, ↓ acne flare-ups

Physiology: ↑ HCA2 receptors, ↑ transient Ca²⁺

Reduces pore size

Cosmeceutical features:

↓ pore size, ↑ unclogged pores, ↑ dermal aesthetic appearance, ↑ healthy skin barrier function

Physiology: ↑ ECM quality, ↑ skin barrier integrity, ↑ mRNA expression of serine palmitoyl transferase, ↑ keratin K1 expression, ↑ fibroblast senescence, ↑ normal fibroblast activity maintenance, ↓ MMP, ↓ elastase, ↑ collagen production

THE CLINICAL POTENTIAL OF TEA TREE OIL

Skin calming agent

Cosmeceutical features:

↓ redness, ↓ swelling, ↓ pain, ↓ acne flare-ups

Physiology: ↓ excessive production of ROS, ↑ GSH levels, ↑ CAT activity, ↓ intracellular H_2O_2 formation

Combined anti-inflammatory and antimicrobial action

Cosmeceutical features:

↓ redness, ↓ swelling, ↓ infection of acne-affected skin, ↑ dermal healing

Physiology: ↓ IL-1, ↓ IL-6, ↓ iNOs, ↓ COX2, ↓ IL-23, ↓ IL-17, ↓ NF-κB, ↓ IL-3, ↓ IL-10, ↓ GM-CSF, ↓ IFN-γ, ↓ IL-1β, ↓ IL-8, ↓ PGE2, ↓ NTPDase, ↑ the intracellular ROS produced by monocytes, ↓ superoxide anion radical formation

Table 1: Classification and clinical significance of cosmeceutical ingredients included in the BioMedical Emporium Anti-Acne Serum

INGREDIENT	CLASSIFICATION	REASON FOR INCLUSION
Retinol	Vitamin A derivate	Improves the epithelization of the skin, improves the appearance of acne scars and helps to normalize the physiology of the epidermis and retain skin moisture
Salicylic acid	βHA, phenolic aromatic acid	Anti-inflammatory action, deep cleaning (keratolytic agent), sebum regulation, skin degreasing properties and reducing pore size
Niacinamide	Water-soluble vitamin, antioxidant	Sebum suppression, anti-inflammatory and healing properties
Tea tree oil	Essential oil obtained from <i>Melaleuca alternifolia</i>	Antibacterial, antifungal, antiviral, anti-inflammatory and scavenger of ROS



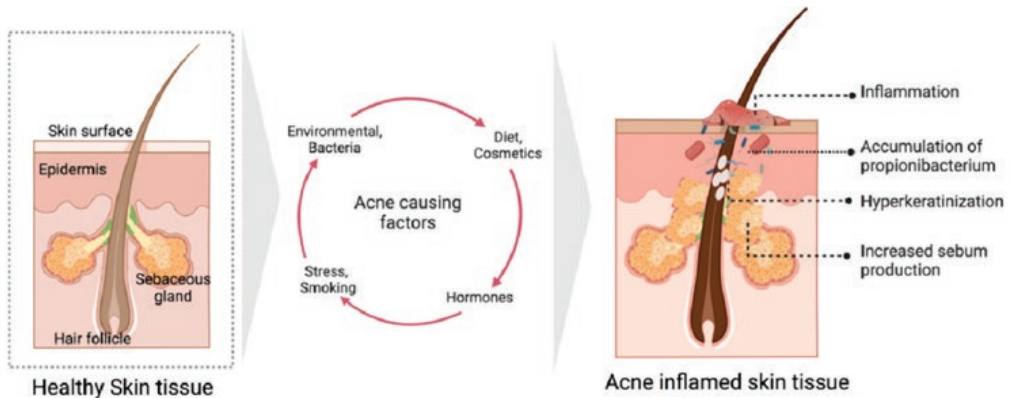


Figure 1. Schematic illustration of healthy/normal skin tissue compared to acne inflamed skin tissue, various factors contributing to the formation and development of acne (Vasam et al., 2023).

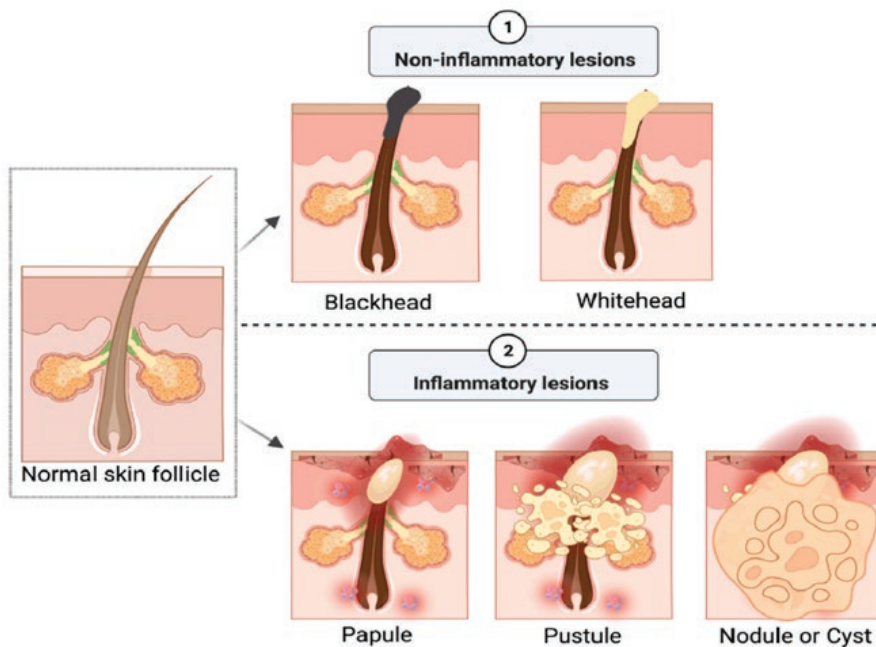


Figure 2. Schematic illustration of major distinguishing of the two types of acne lesions (non-inflammatory, inflammatory) and their pathogenies (Vasam et al., 2023).

ABBREVIATIONS

ACC:	acetyl coenzyme A carboxylase
AMP:	antimicrobial peptide
AMPK:	5' adenosine monophosphate-activated protein kinase
AP-1:	activator protein 1
βHA:	beta-hydroxy acid
BCL6:	b-cell lymphoma 6
Ca²⁺:	calcium ions
CAT:	catalase
COX-2:	cyclooxygenase-2
CSF:	colony-stimulating factor
ECM:	extracellular matrix
FAS:	fatty acid synthase
GM:	granulocyte-macrophage
GSH:	glutathione
H₂O₂:	hydrogen peroxide
HCA2:	hydroxycarboxylic acid receptor 2
IL:	interleukin
IFN:	interferon
iNOS:	inducible nitric oxide synthases
LL-37:	cathelicidin antimicrobial peptide
MHC:	major histocompatibility complex
MMP:	matrix metalloproteinases
MRC:	mannose receptor C

mRNA:	messenger Ribonucleic Acid
NAD⁺:	nicotinamide adenine dinucleotide
NF-κB:	nuclear factor κB
NOS:	nitric oxide synthase
NTPDase:	nucleoside triphosphate diphosphohydrolase
OSM:	oncostatin-M
PARP:	poly (adenosine diphosphate ribose) polymerase
PGE₂:	prostaglandin E ₂
RARs:	retinoic acid receptors
ROS:	reactive oxygen species
RXRs:	retinoid X receptors
SASP:	senescence-associated secretory phenotype
SIRT:	sirtuin
STAT3:	signal transducer and activator of transcription 3
SREBP:	sterol response element-binding proteins
TLRs:	toll-like receptors
TNF-α:	tumor necrosis factor-α

WARNINGS

Inappropriate or excessive use of topical retinol can lead to potential side effects. These generally include skin dryness, redness, and peeling which can cause discomfort. However, typically these side effects diminish over time as the skin adjusts. Therefore, lower doses of retinol can be applied until the skin tolerability improves whereafter the concentration of retinol can be increased. Please note: BioMedical Emporium Anti-Acne Serum contains vitamin A-related compounds, which contributes to the daily intake of vitamin A.

Sun alert: Vitamin A-containing products may cause photosensitivity and increase sensitivity to sunburn, so be certain to apply adequate sunscreen protection while using BioMedical Emporium Anti-Acne Serum.

Topical salicylic acid formulations are generally well-tolerated by all skin types. However, salicylic acid application should be avoided in individuals with salicylate allergy, active dermatitis, and skin infections. Avoid using salicylic acid in combination with an agent that causes dry skin (some individuals can be more sensitive to experiencing dermal dryness). Topical use of salicylic acid during pregnancy is not associated with an increased risk of congenital

malformation as is the case with systemic salicylic acid administration due to its structural similarity to aspirin. It is recommended to limit the size of the area exposed to salicylic acid, avoid occlusion of the site where salicylic acid is applied, and limit the duration of topical salicylic acid use during pregnancy.

Side effects from the topical application of niacinamide are minor and rare and niacinamide is generally a well-tolerated and safe substance often used in topical applications. Reported side effects may include mild burning, pruritis, and erythema. However, these side effects tend to improve with continued use.

The volatiles that constitute tea tree oil can penetrate the skin or increase penetration of other compounds and trigger toxicity. Severe reactions can be considered extremely rare in the absence of ingestion, although some components of tea tree oil are responsible for some allergic reactions (i.e., 1,8-cineole, terpinen-4-ol, limonene).

STORAGE INSTRUCTIONS

This product is packed in an airless, opaque container, providing protection from oxygen exposure and ambient light. Store at or below 25°C.

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