Trioxil.**AM**™ & Trioxil.**PM**™ Acne Treatment

Technical Data Sheet

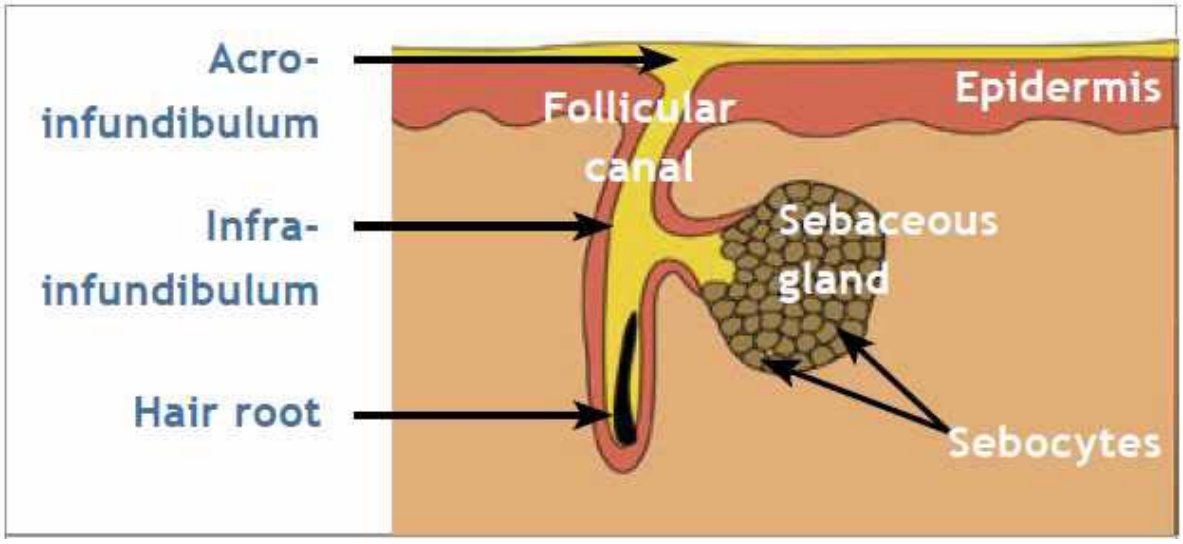
Trioxil.AM™ and Trioxil.PM™ are designed to work together to provide a broad multi-lateral attack on acne by addressing the core pathology of acne though the keratolytic, anti-seborrheic, and anti-inflammatory properties.

Introduction

Acne describes a condition in which the pilosebaceous follicle is inflamed. Therefore, it is a kind of folliculitis and its causes can be either endogenous or exogenous. Sebaceous hair follicles which are mainly found on the face and the upper chest and back are the only ones which are subject to this kind of inflammation.

This skin condition is very common around the time of puberty when it is referred to as common acne or acne vulgaris. It effects almost 90% of young people with severe involvement seen in 50% of 14 year olds and 78% of 16 year olds.

Pilo-sebaceous follicle

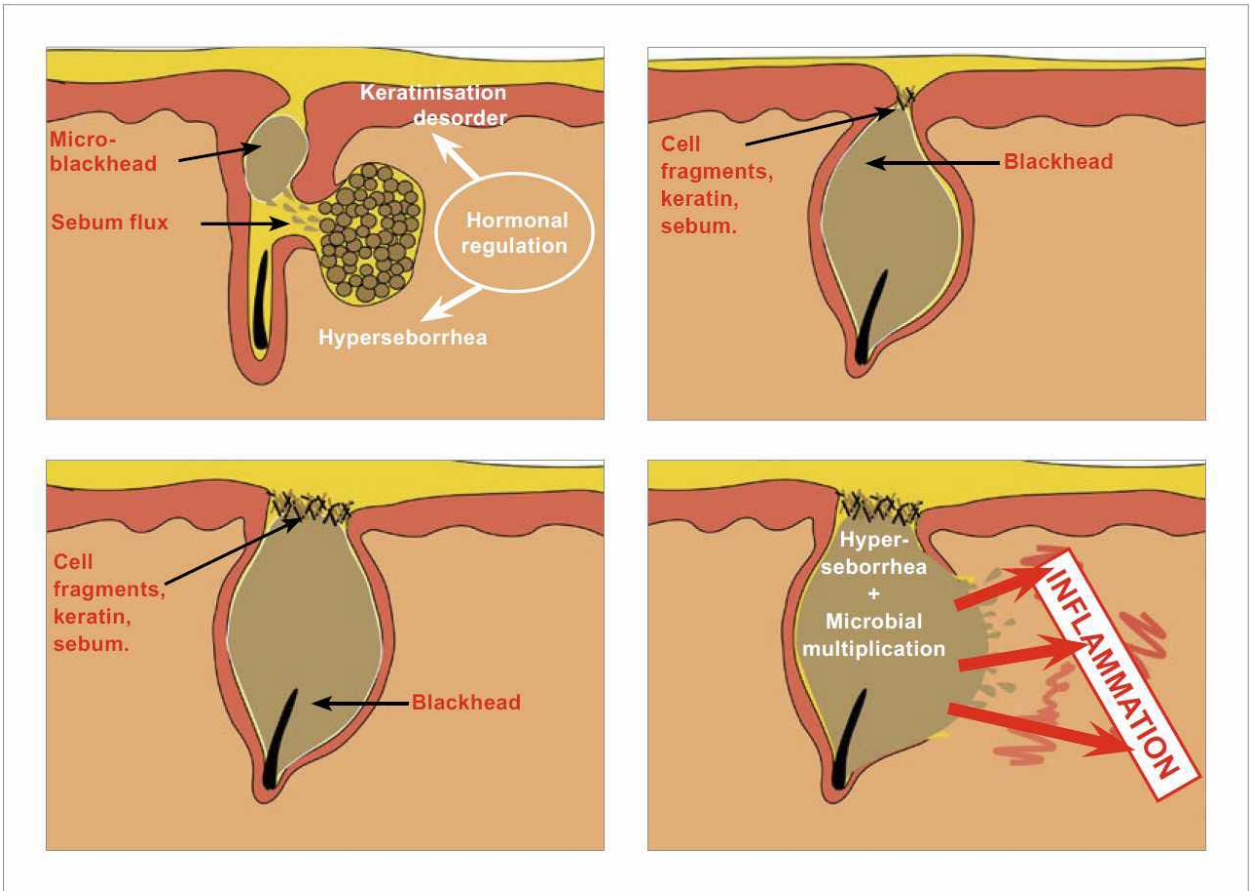


Pilosebaceous follicles are found all over the skin, everywhere except the finger and toenails, the palms of the hands and soles of the feet. They are most dense on the face and the upper chest and back. Sebum is produced by the disruption of sebocytes, full of lipidic matter, into the sebaceous gland. Sebum contains the following substances: triglycerides, di-mono glycerides, free fatty acids, waxy components, squalene, and cholesterol.

The pathology of acne

Acne is a disorder of the pilosebaceous unit and its etiology involves multiple factors, of which the main three are:

1)Seborrhea 2)infundibular hyperkeratinization 3)inflammation of the follicle



1. **Seborrhea**

It is a central factor in the pathogenesis of acne. It results from changes in the levels of the androgens, a group of hormones which are very important in the regulation of the sebaceous gland metabolism. These changes can result from loss of normal regulation depending on the rate of secretion of hormones, their transport in the plasma, and how they are metabolized intracellularly.

In certain pathological conditions, the rate of synthesis and secretion of androgens like testosterone tends to increase. In the sebaceous gland, testosterone is intracellularly converted to DHT by the action of the enzyme 5α-reductase therefore increasing circulating testosterone levels which lead to increased intracellular concentrations of DHT. This stimulates protein synthesis and the rate of sebum secretion increases.

Once secreted, androgens are transported around the body in the blood. They are not transported as free hormone but rather conjugated with a special protein, Sex Hormone Binding Globulin (SHBG).

Androgen metabolism depends on three key enzymes, namely 3-β-hydroxysteroid dehydrogenase, 17-β-hydroxysteroid dehydrogenase and 5α-reducatase. Enhanced activity by any of these will raise intracellular DHT levels inside sebum producing cells and stimulate sebum secretion.

2. Hyperkeratinization

The comedo is the fundamental lesion of acne and arises when, as a result of the over-production of keratin, a plug of keratin and sebum blocks the infundibulum of the hair follicle which as a consequence becomes dilated. Comedo formation can be divided into three different stages:

- Microcomedo: only visible by microscope
- The closed comedo or “whitehead” corresponding to an accumulation of sebum and keratinized cells. These lesions may burst and induce a polymerphonuclear inflammatory response when various bacteria and fatty substances are released
- The open comedo or “blackhead” due to ongoing production of keratinized cells and sebum, the follicular orifice becomes dilated and can develop into inflammation, sometimes bursting spontaneously.

3. Follicular inflammation

Bacteria are involved in the inflammatory process. Although they are not the primary etiological agent, they play an important role in the subsequent, secondary inflammatory reaction. The natural flora of the pilosebaceous follicle consists of three different types of microorganism: Propionibacteriae, Micrococcaceae, and Pityrosporum orbiculare.

The most important member of the Propionibacteriae family is Propionibacterium acnes which colonize the lower reaches of the follicle. It has strong enzyme activities (lipases, proteases and hyaluronate-lyases) and contains “histamine-like” and “prostaglandin-lie” substances.

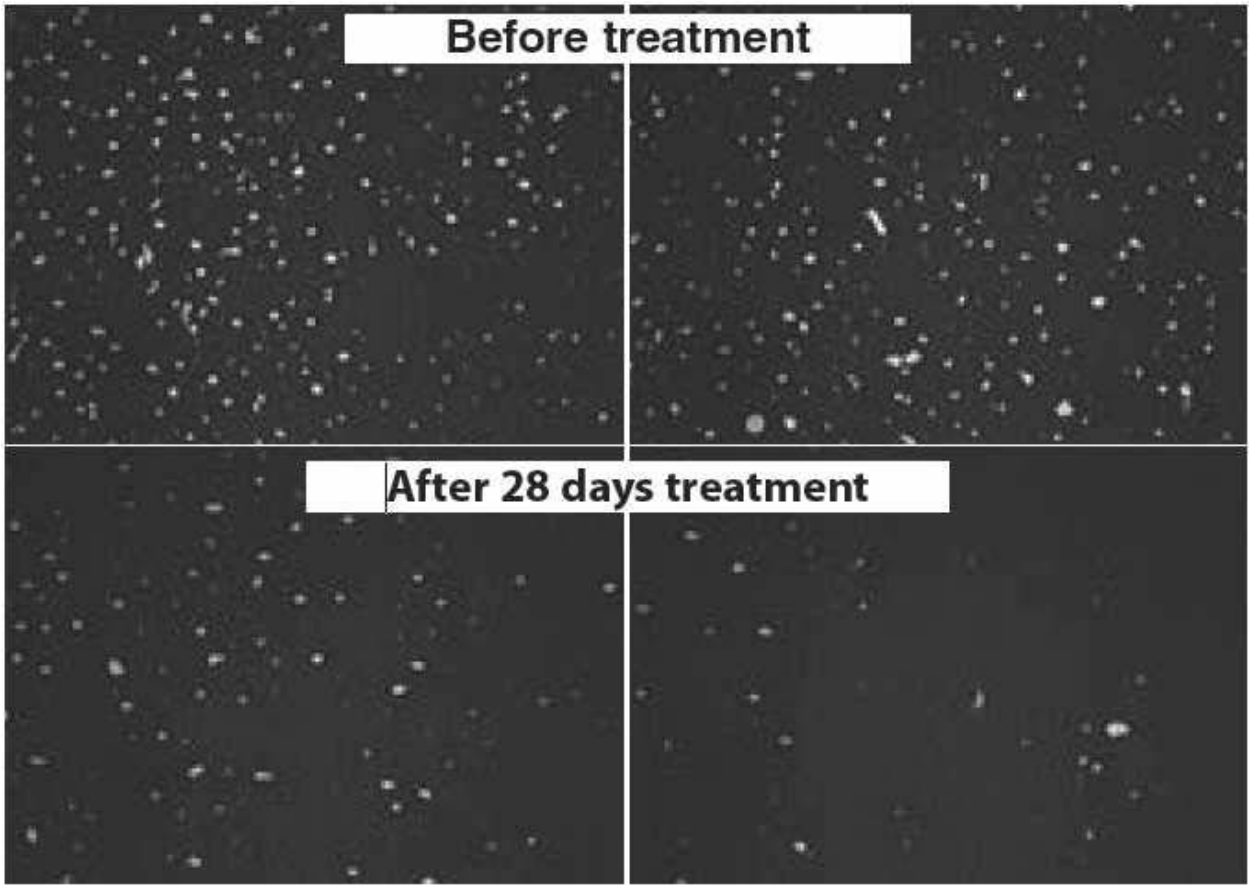
Among the Micrococcaceae, the Staphylococcus epidermidis can mediate perifollicular elastolysis which can lead to scarring. Finally, Pityrosporum orbiculare is a lipophilic yeast which contains strong lipase, phosphatase and proteinase activities. It is common in acneform lesions, especially in the closed comedo.

Efficacy

Sebum regulating effect

After 28 days of use of Trioxil.PM™ , the sebum regulating affect was tested with Sebutape. Trioxil.PM™ significantly reduced the number of over-active sebum glands. Additionally the total flow of sebum was also significantly reduced.

Placebo Trioxil.PM™



Evaluation of the number and size pf the active sebaceous glands/sebum spots on Sebutape.

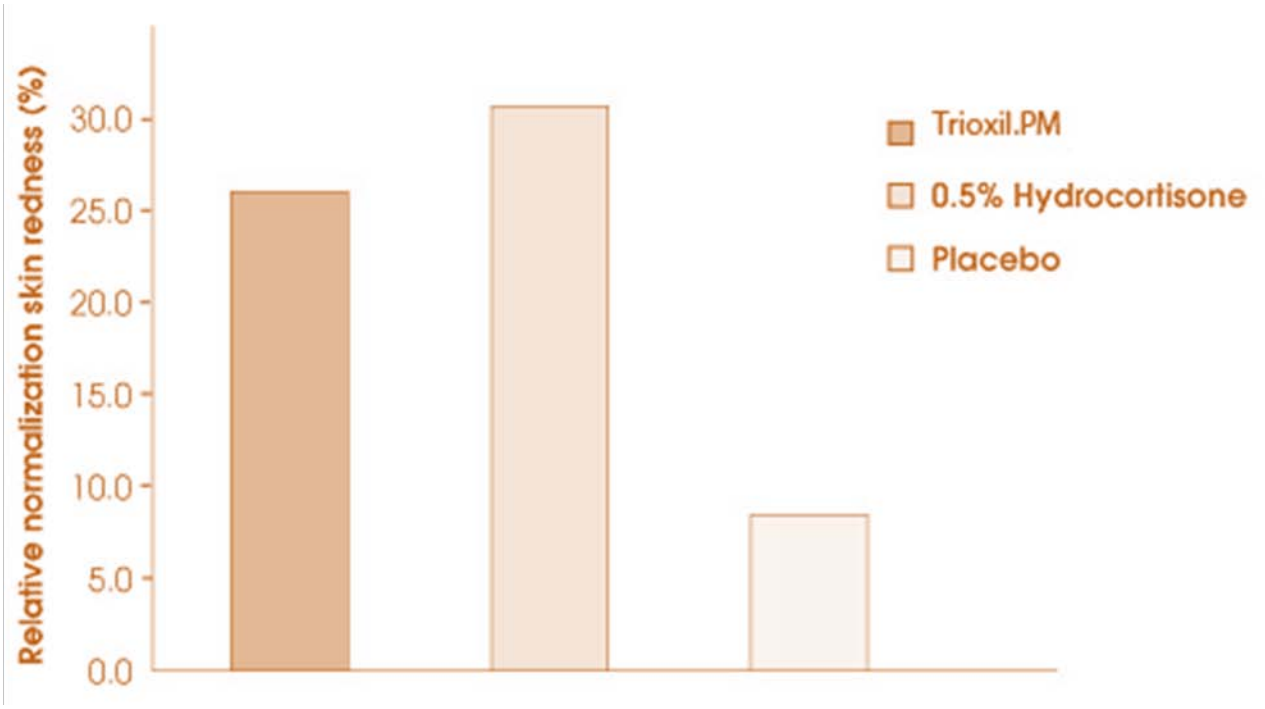
Anti-bacterial effect

As described previously, accumulated sebum is a perfect breeding place for bacteria (above all Propionibacterium acnes). By means of certain enzymes (lipases) these bacteria are able to decompose sebum under formation of free fatty acids. Free fatty acids in turn penetrate the surrounding tissue and provoke inflammatory phenomena as redness and pimples.

Trioxil.PM™ has shown to effectively target excessive microbial colonization and secretion of sebum, with simultaneous anti-irritant action.

Anti-inflammatory action

The anti-irritant or anti-inflammatory action of Trioxil.PM™ could be demonstrated vividly in the UVB erythema test. The skin redness of test persons was reduced equally by treatment with Trioxil.PM™ , cream with 0.5% of hydrocortisone, and placebo.



On the cellular level it could be observed that Trioxil.PM™ is able to inhibit the activity of enzymes that catalyse formation of inflammation mediators. Inflammation mediators are involved in development of inflammation (e.g. redness). In presence of Trioxil.PM™ the enzyme 5-lipoxygenasis, for example, is inhibited in a concentration dependent way whereby formation of inflammation mediator LTB4 is impaired considerably.

Anti-microbial action

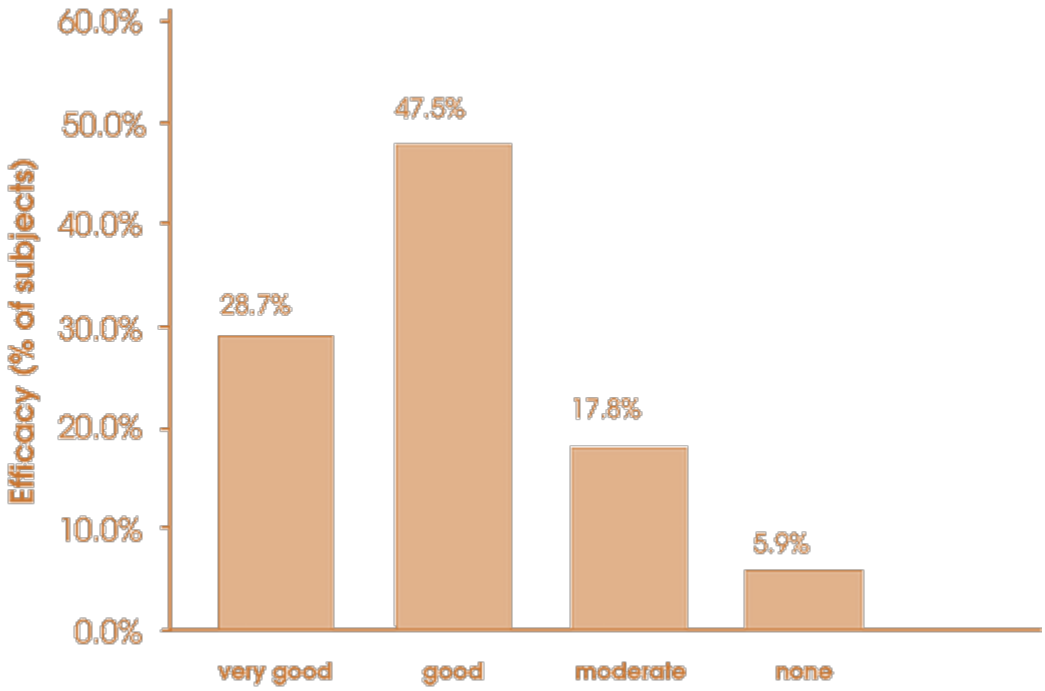
Trioxil.PM™ features anti-microbial action in all germs that are relevant in acne problems. Regarding Propionibacterium acnes Trioxil.PM™ is highly active.

Effect of Trioxil.PM™		
MICRO-ORGANISM	**MIC (%)**	**INHIBITING ZONE DIAMETER (mm)**
Staphylococcus aureus	0.039	1.0
Pseudomonas aeruginosa	0.039	0.5

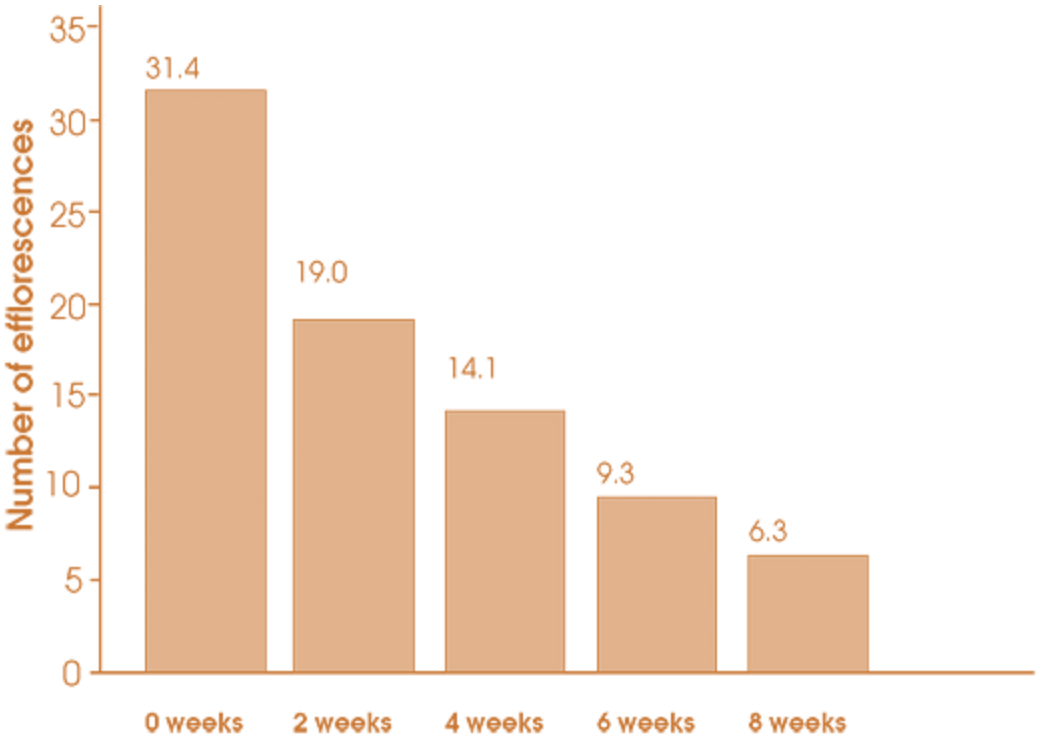
Pityrosporum spec.	-	2.0	
Candida albicans	0.2-5.1	-	-
Dermatophytes (p. ex. Microsporum canis, Trichophyton rubrum)	0.05-0.1	-	-
Propionibacterium acnes	0.039	-	-

Global treatment of skin blemishes

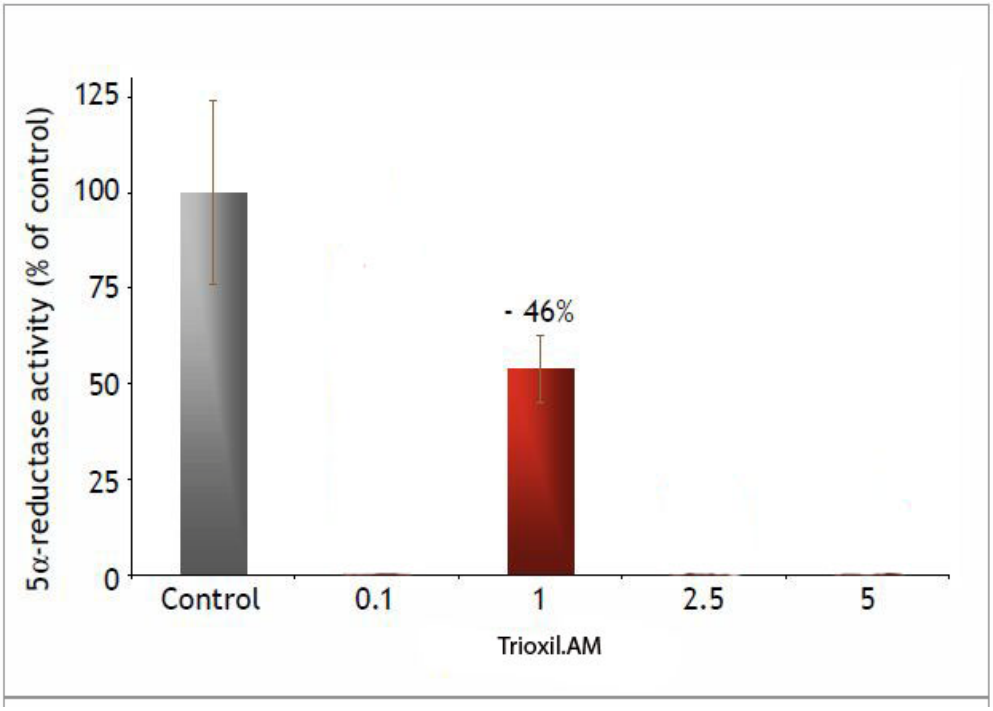
Combining anti-inflammatory and anti-microbial properties, very good effects are achieved in elimination of acne. This result was arrived at in a study conducted in 101 test volunteers who were treated with one of the key ingredients in Trioxil.PM™ . After a treatment phase of six weeks the efficacy was evaluated as “good” or “very good” in 76% of all cases.



In another study the efficacy of Trioxil.PM™ and 0.5% of salicylic acid was examined. In course of the treatment phase of eight weeks the average number of visible efflorescences could be reduced from 31.4 to 6.3 corresponding to a decrease of about 80%.



5α-reductase reduction



When measured in human dermal fibroblast cultures, ingredients in Trioxil.AM™ reduced the activity of 5α-reductase by 46%, which is the principle agent in acne pathogenesis.

Conclusion

Trioxil.AM™ and Trioxil.PM™ working in combination address all the main components of acne pathogenesis and deliver this effect without irritation or disruption of skin's natural balance. These acne gels stimulate the natural defense functions of the skin, combat microbial infections, normalize sebum production, and limit inflammatory reactions of the skin. Extensive clinical testing has shown a dramatic global improvement in the appearance of acne when used as directed.