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# Cosmetics Insights into Acne



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# COSMETICS INSIGHTS INTO ACNE

## INTRODUCTION

Acne Vulgaris is an inflammatory disease that leads to physical as well as mental stress for many people. Approximately 90% of teenagers worldwide experience Acne [1,2]. Most people who experienced [MS(1)] Acne are reminded of many insecure hours in front of the mirror. People often do not feel comfortable when their skin is decorated with pustules [3]. Despite that so many people struggle with Acne at some point in their life, it is still a blur what Acne actually is. We will discuss standard treatments and new, innovative, and more efficient skin microbiome-derived treatments. As you will discover, the beauty industry plays a crucial and promising role in the treatment of Acne.

## BACKGROUND

### SKIN BIOLOGY

Acne is a disease located on our biggest organ, the skin. The skin is often taken for granted and this sometimes lets us forget that the skin has some essential functions [4]:

- Protecting our inner tissue
- Regulating the temperature
- Sensorial activity
- Adjusting to big volumes, like pregnancy
- Vitamin D synthesis
- Attractiveness

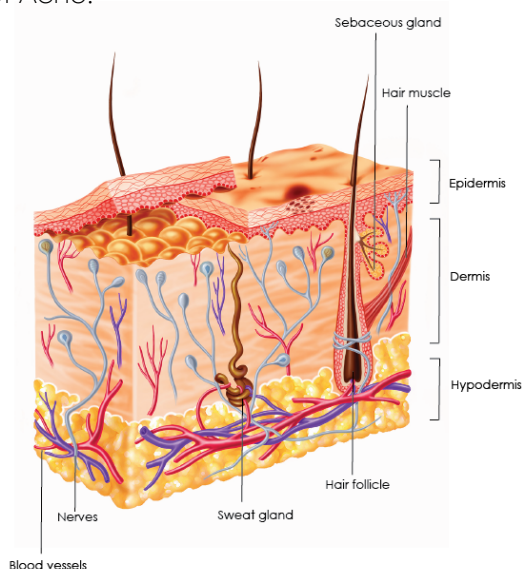


Figure 1 **The layers of the human skin are schematically illustrated [6,7].** The hair follicle and sebaceous gland are outlined.

The skin consists of the epidermis and the dermis (Figure 1). The primary cell type in the epidermis is the skin cell. They multiply at the bottom of the epidermis and migrate to the surface to form a protective layer. You can compare it with a beer head. The foam layer grows from the bottom and after a while, the foam disappears on the top. This happens with the skin cells as well. The skin cells maintain the skin intact from underneath and after one and a half months the skin cells desquamate on the surface. The dermis is the deeper layer and is filled with several biologically active components [4]:

- Blood vessels
- Sweat glands
- Hair follicles
- Sebaceous glands



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The sebaceous gland is the villain from the above's list during Acne. The sebaceous gland consists of a hollow space with a duct that is connected to the hair follicle (Figure 1). Sebum is a mixture of squalene, triglycerides, wax esters, cholesterol, fatty acids, and vitamin E [5]. It is released when cells of the gland burst open like a water balloon, secreting the cellular contents and the remains of the cell together. The function of the sebum is [4]:

- Lubricating the skin
- Hydrating
- Anti-microbial activity
- Regulating temperature
- Antioxidant activity
- Pro- and anti-inflammatory
- Protecting against UV-radiation
- Maintaining the skin microflora

## WHAT CAUSES ACNE?

Unfortunately, we cannot pinpoint one single cause of Acne. First, genetics affect if a person is susceptible to Acne. In addition, many other factors are important as well, such as [8–13]:

- Increased sebum production (hyper seborrhea)
- Rapid shedding of skin cells (hyperkeratinization)
- Increased growth of *Cutibacterium acnes*
- Inflammation
- Oxidative stress

### COMEDUNAL (NON-INFLAMMATORY)



### PAPULO-PUSTULAR {INFLAMMATORY}



### NODULAR {INFLAMMATORY}



Figure 2 **The three types of Acne.** The comedonal (non-inflammatory) type is characterized by whiteheads, a closed comedo (clogged hair follicle), and blackheads, an open comedo. The second Acne type consists of papules, small bumps that are less than 5mm in diameter, and pustules, smaller bumps with a visible central core of purulent material. The final Acne type consists of nodules, which are bumps greater than 5mm in diameter.

For those who wondered why Acne often strikes during puberty, the ones to blame are hormones. Hormones are messenger molecules that inform a cell what it should do. DHEA-S is a hormone that increases sebum production. However, during puberty, it is like someone is spamming the sebaceous gland with the request to produce massive amounts of sebum. This is because the secretion of DHEA-S is increased during puberty [14]. Sebum is a superfood for *C. acnes* while the other protective microbes do not like sebum. The sebum-rich environment supports *C. acnes* to become the dominant species of the skin microbiome. *C. acnes* is initially a major protective microbe, but all that sebum changes its gene expression or leads to a loss of healthy *C. acnes* strains. Sebum transforms *C. acnes* from an ally into an enemy of the skin. There are three main types of Acne based on the symptoms (Figure 2).

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## CLOGGED HAIR FOLLICLES CALLED COMEDONES (FIGURE 3)

- Whitehead: closed comedo
- Blackhead: open comedo

## PAPULO - PUSTULAR

- Papules: bumps smaller than 5.0 mm
- Pustules: small bumps with a visible central core

## NODULAR

- Nodules: bumps bigger than 5.0 mm

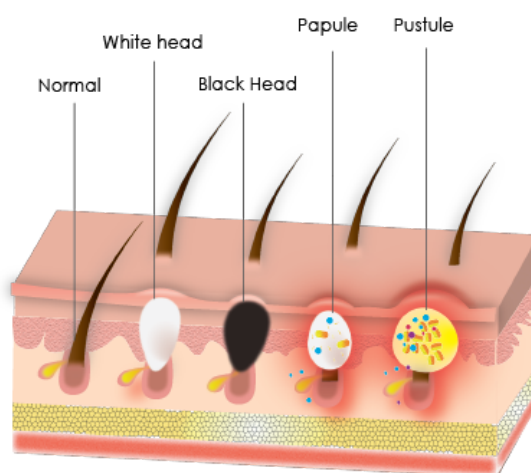


Figure 3 **The self-regulating power of the skin microbiome is completely lost.** *C. acnes* and to a lesser extent *S. epidermidis* have a free hand. They behave like dictators.

All these bumps in the skin are caused because the **sebum** accumulates in the narrow duct that transports sebum to the surface. This leads to pressure on the skin cells. The skin cells push back by producing more skin cells. Unfortunately, all this violence has only one outcome: the formation of a pustule, because the only space left is upwards.

A **comedo** that did not burst yet is the most ideal situation. It naturally isolates the Acne war that is going on. In contrast, when a comedo does break, bacteria infiltrate the skin, territory where they are not supposed to be. The immune cells in your skin become active and the inflammation creates this typical red area around the pustule. Inflammation was one of the factors that contribute to Acne, therefore Acne is again boosted by inflammation.

The open comedo is called a **blackhead**. When *C. acnes* becomes more active, it starts a pathway that leads to a change in the sebum composition. The sebum becomes a wax and it loses its liquidity. The dark color is caused by the oxidation of the wax. Here, *C. acnes* really starts to torture our beautiful skin. The oxidized wax acts as a biofilm, which creates an anaerobic environment over the skin. Without oxygen, the growth of *C. acnes* and *Staphylococcus epidermidis* goes even faster, resulting in a destructive feedback loop for our skin and for the remaining protective skin microbiome. [15]

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## ACNE TREATMENT

There are a few absolute no-goes with respect to Acne treatment. First, do not remove sebum. When you remove sebum, the sebaceous gland thinks that it did not work hard enough and it starts to produce even more. Second, do not remove pustules. By removing pustules you damage the gland and this also accelerates Acne development. Finally, it is hard to resist, but do not aggressively peel the skin. Peeling spreads *C. acnes*. You may question: "Which options are available for Acne treatment?" Here, we will discuss several popular treatments that all target one of the main causes of Acne: increased sebum production, hyperkeratinization, increased bacterial growth of *C. acnes*, and inflammation.

### **Benzoyl peroxide**

Products for Acne care are available with and without a prescription. Benzoyl peroxide is among the most popular drugs against Acne in the pharmaceutical industry. It kills bacteria, is anti-inflammatory, and prevents the formation of clogged hair follicles. The main mechanism is that benzoyl peroxide makes the place where *C. acnes* grows more aerobic. *C. acnes* does not prefer oxygen and therefore making this drug very effective. Benzoyl peroxide shows typically already result after several days of treatment. However, benzoyl peroxide has some disadvantages, especially for people with sensitive skin [12,13]:

- Irritation
- Dryness
- Burning feel
- Red skin
- Bleaching of clothes, hair, and bed linen

### **Retinoids**

Retinoids are another option in Acne treatment and have been used for over three decades. Retinoids are a vitamin A derivative. Retinoids are effective against the formation of clogged hairs by reducing the sebum and are an ideal choice as a first-line therapy. There are still some disadvantages when using retinoids [12,13]:

- Dryness
- Burning feel
- Red skin
- Scaling
- Unsuitable during pregnancy or five years prior to a planned pregnancy – it may misform the fetus.
- Photosensitivity – it is recommended to use sunscreens



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## **Salicylic Acid**

Salicylic acid is a molecule with the ability to reduce the production of lipids by the sebaceous gland cells. In addition, it reduces inflammation. Both are crucial factors in Acne development. Next, the molecule is also able to kill sebaceous gland cells in a regulated manner to decrease sebum production [16]. Finally, salicylic acid can gently remove the outer layer of the skin. This aids in helping the pores stay open and prevent that there will be an anaerobic environment beneficial for *C. acne* and *S. epidermidis*. So, salicylic is a real hero and capable to treat Acne on many levels.

## **Zinc**

As explained, sebum production is regulated by hormones. The most straightforward solution to reduce sebum production would be to stop sending signals to the sebaceous gland. Zinc derivatives are very effective because they approach the problem by the source; they inhibit the enzyme that makes the hormone for sebum production (5 $\alpha$ -Reductase); no messages mean no sebum [ 17]. Imagine that someone missorts all the letters at the post office; none of the messages will reach their destination. One of the most popular choices to have this effect is zinc Pyrrolidone Carboxylic Acid (Zn PCA). In addition to inhibiting hormone production, it also has antimicrobial properties against *C. acnes* and *S. epidermidis* [18].

## **Azelaic Acid**

Azelaic acid is a super soldier in the fight against Acne. It is able to target all major factors that aid in Acne development. It slows hyperkeratinization by very delicately removing skin cells. Skin cells are connected with desmosomes. These desmosomes are like hands that hold each other. Azelaic acid breaks this bond in such a gentle way that it does not break the skin. Next, azelaic acid inhibits the formation of the main hormone that regulates sebum production. Finally, this allrounder has the ability to kill bacteria [17,19].

## **Antibiotics**

Another common treatment for Acne is antibiotics. Antibiotics are commonly used in combination with benzoyl peroxide. Antibiotics stagnate the growth of bacteria or even kill them. Killing bacteria sounds wonderful, but those that survive evolve to become resistant to the antibiotic [20]. This means that the antibiotic loses its effectiveness. Another big impact is that with antibiotics you severely bring your skin microbiome out of balance [21]. This brings us to a very important player in skin care: the skin microbiome.

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## **Skin microbiome**

An innovative solution to Acne care is found in the skin microbiome. The skin microbiome is a resourceful layer of the skin that houses up to 1,000 microbial species that all communicate with each other for survival [22]. The skin microbiome and the skin are in a perfect marriage. They both rely on each other in order to survive. In a healthy state, *S. epidermidis* limits the over-colonization and inflammatory response of the skin by *C. acnes*. *S. epidermidis* is like the gardener who occasionally prunes the trees such that they do not grow too big. *C. acnes* in his turn suppresses the proliferation of *Staphylococcus aureus* and *Streptococcus pyogenes* [23]. The skin microbiome draws its energy and power from the balance between all the species and the communication between all of them. The skin microbiome behaves like a big hive.

However, this natural balance is broken during Acne. Acne's severity is related to a loss of *C. acnes* strain diversity [24]. Imagine that everyone drives identical cars. Suddenly, the manufacturer tells that a specific part of the braking system is unsafe. Everyone is now susceptible to an accident and nobody has then an alternative. It is much safer (or healthier) if there is a diverse set of cars (more and different *C. acnes* strains). In Acne, one specific strain becomes very dominant [22,24]. The question now is, can we assist our skin microbiome in maintaining its diversity and balance for Acne-prone skin? Can the balance be repaired and the diversity be increased back to a healthy level? Or in other words, can we stimulate our skin population to invest again in many different cars? Moreover, can the microbiome be stimulated to invest in bikes, boats, and planes? All the friendly microbes are suppressed, so we want this diversity back.



## **PreBIULIN® FOS**

There are promising developments in the cosmetic industry; an industry where brands used to focus on killing bacteria. Fortunately, brands are becoming aware of how important it is to maintain the microbial balance to keep our skin beautiful and healthy. The microorganisms of the skin microbiome are irreplaceable because they:

- Protect us from harmful bacteria
- Offer sun protection,
- Provide anti-cancer molecules
- Produce anti-oxidants
- Hydrate the skin using a biofilm
- Work with our immune system

This emphasizes again that the microbiome should be the primary target to treat skin disorders, such as Acne. Reducing or killing the villain, the pathogen, is not enough as this does not restore the protective microbiome.

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An efficient solution is to include prebiotics in cosmetic formulations. Prebiotics support selectively the activity and growth of beneficial skin microbiota [25]. You can compare prebiotics to rewarding your employees with a Christmas bonus. You do not give the bonus to the people that you do not want in your company. They will not be happy and do not come back after Christmas. This group is the bacteria that do not belong on your skin. You solely reward the true residents of the skin microbiome. So, by promoting your skin microbiome, you will also indirectly eliminate unwelcome guests. This keeps the balance intact and makes the community stronger.

An ingredient with this prebiotic activity that has been proven as an excellent candidate for Acne-prone skin is PreBIULIN® FOS. PreBIULIN® FOS consists of processed inulin (GF10) that is extracted from the chicory root [26]. Inulin is a long molecule of fructose units chained together.

A study with a 1% PreBIULIN® FOS mixture on Acne-prone skin shows that *C. acnes* and *S. epidermidis* became less dominant, while the protective microbiome recovered (Figure 4A). What is even more amazing is that this study used a rinse-off product. These bacteria are both overly present during Acne and disturb the skin microbial balance. In addition, this study shows that bacteria that are considered as healthy increased in their number. These results are remarkable and show us that by supporting our skin microbiome, instead of merely killing *C. acnes* directly, Acne can be treated (Figure 4B). The same study also showed that washing the Acne-prone skin with a facial wash without PreBIULIN® FOS improves only the dominance of the villains, while the protective microbiome is significantly reduced. Each time the Acne-prone skin is washed, you wash away your last chance to combat the Acne villains.

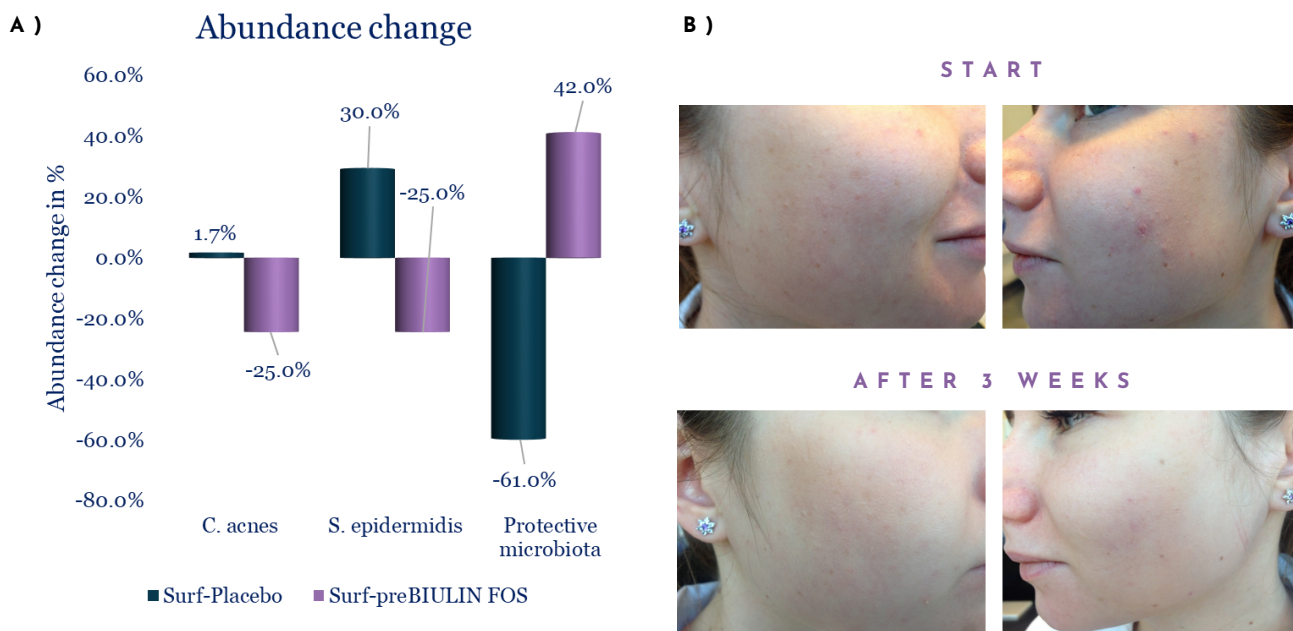


Figure 4 **A Microbial abundance change after treatment with a 1% PreBIULIN® FOS mixture.** The abundance change was determined by comparing the microbial composition before treatment and after two hours of treatment. The abundance change is defined as the percentage change from the initial count. The abundance was determined for *C. acnes*, *S. epidermidis*, and known bacteria that are labeled as protective. **B Testimonial of a female with acne-prone skin before and after a three-week daily use of a 1% PreBIULIN® FOS formulation.**



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A balanced skin microbiome can be compared to a big social media network. Every single specie cooperates and communicates with other species. During Acne, there is a power outage. Species fail to communicate with each other. To check if this communication can be restored with preBIULIN® FOS, a follow-up metagenomics study was done. This study analyzes all the microbial DNA of the skin and answers the question: “Who is there and how do they interact with each other?” Interaction networks were constructed for the microbiome before and after treatment with either a placebo or a 2% preBIULIN® FOS formulation (Figure 5A-D). Each node in the network represents a bacterial species and an edge means that two species interact with each other. The result was astonishing, showing an increment of over 12,000 restored interactions when using preBIULIN® FOS, while the placebo did not even exceed a total of 5,000 interactions. Moreover, the species diversity was higher when using preBIULIN® FOS (Figure 5E). This means that the power outage is restored. Finally, the microbial composition of the skin shows that the presence of the dominant species in Acne, *C. acnes*, dropped by 33% (Figure 5F). The *C. acnes* population normalized again. All these results together tell us that preBIULIN® FOS aids in restoring microbial balance and the communication of the skin microbiome.

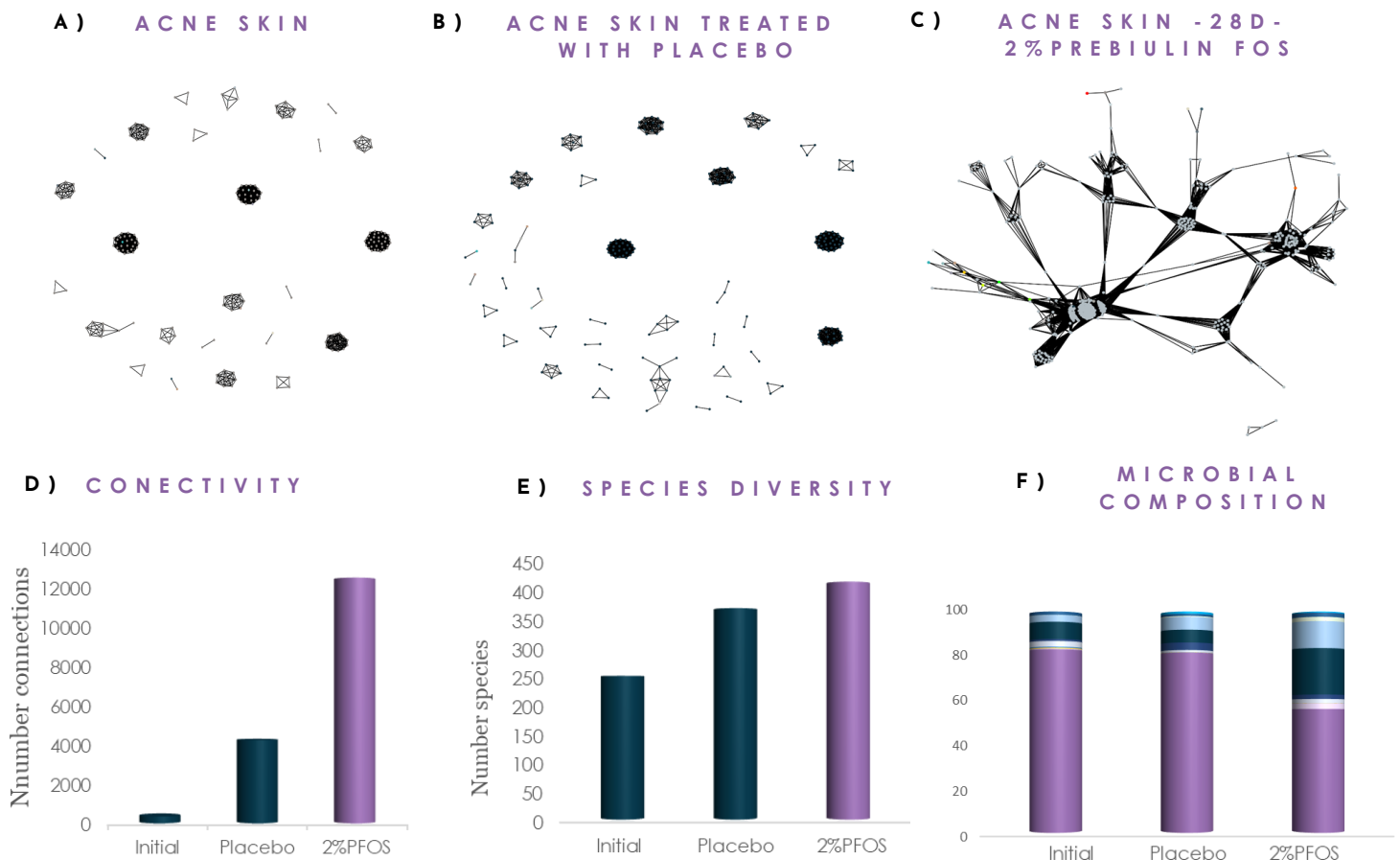


Figure 5 **A, B, C** Communication network for all the present bacteria of the skin microbiome in Acne skin, Acne skin treated without PreBIULIN® FOS, and Acne skin treated for 28 days with a 2% PreBIULIN® FOS formulation, respectively. **D** A quantification of the number of connections for the networks in figures A, B, and C. **E** The number of unique bacterial species before and after 28 days of applying a formulation of 2% PreBIULIN® FOS. **F** The microbial composition of the skin before and after 28 days of applying a formulation of 2% PreBIULIN® FOS.

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## Gosulin® Rice

A second cosmetic ingredient that has proven to be of aid against Acne is Gosulin® Rice [27]. Gosulin® Rice consists of heat-treated rice starch. The heat treatment enlarges the pores that are present in the rice particles. These pores have the unique property to absorb oil and this is exactly the strength of Gosulin® Rice against Acne. In fact, Gosulin® Rice is able to absorb almost 90% of oil compared to its own weight (Figure 6). It is a big sponge for oil that is also very easy to produce.

For the above's reasons, Gosulin® Rice is an ideal material to remove blackheads. Blackheads are a type of clogged hair follicle on the surface that is open. The blackhead is filled with an excess of sebum and dead skin cells [28]. Gosulin® Rice showed that blackheads are completely and immediately decapitated at a dosage of 25% (Figure 7). An additional perk is that Gosulin® Rice does not remove the root of the clog. By removing the root, the sebaceous gland is stimulated to produce even more sebum. Using Gosulin® Rice for 1 week, twice a day leads to a reduction of the pore size by 60%. Thus Gosulin® Rice is an excellent option if you are in search of an executioner for your red skin torture.

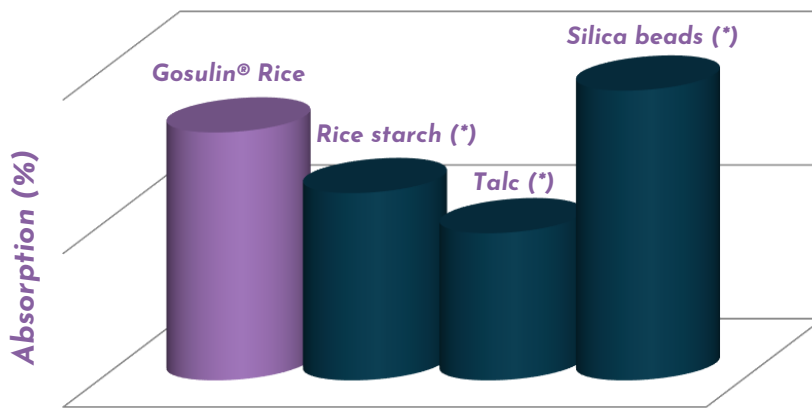


Figure 6 The oil absorption for Gosulin Rice, Rice starch, Talc, and silica beads. The oil absorption was determined by incubating the different materials with jojoba oil. The absorption percentage is the ratio of jojoba oil weight that is absorbed compared to the weight of the material

## Conclusion

In the world of Acne treatment, a big shift from traditional methods to new innovative methods is observed. These methods cause no side effects and are experienced more pleasantly by the user. One of these new methods is to target Acne indirectly via the skin microbiome. Prebiotics boost your skin microbiome to maintain its natural balance. Another good strategy is absorbing sebum, the superfood for *C. acnes*, to remove blackheads. With these new insights, we make promising steps forward in treating Acne-prone skin.



Figure 7 Comparison of blackhead removal between a 10% surfactant formulation and a 25% Gosulin Rice formulation. The comparison was done before applying the formulation and after one hour.

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