

# ACNE GUIDE

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— COSMETIC CLINIC —

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# ACNE

Acne is an inflammatory skin condition that affects up to 80% of 18-30 year-olds and 5% of people over 30 years-of-age [1]. It is commonly experienced on areas of your body that have a high number of oil glands, including your face, back, and chest.

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## WHAT CAUSES ACNE?

There are four main factors that overlap to cause acne. These are:

- Excessive oil production
- The build-up of dead skin cells on the surface of your skin
- A bacteria known as *Cutibacterium acnes*
- Inflammation as part of an immune response to the bacteria.

Your hormones largely control how much oil is produced by your oil glands and hormonal changes or fluctuations can lead to excessive oil production.

Increased oil production, alone, does not cause acne. However, when it's accompanied by a reduced rate of skin cell turnover, dead skin cells can build up on the surface of your skin and trap this oil within your pores.

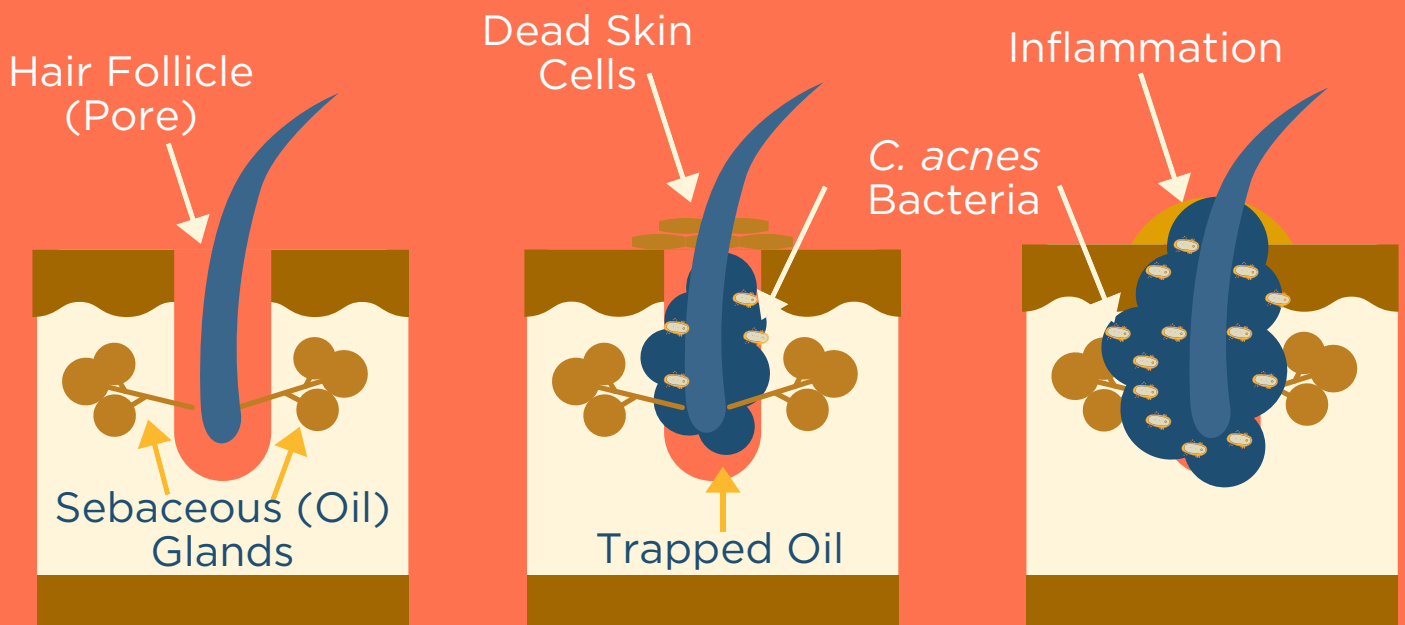
The *C. acnes* bacteria are naturally present on your skin and are normally not an issue. However, because the *C. acnes* bacteria feeds off of your skin's natural oils, when there is an accumulation of oil with no means of escape, the *C. acnes* bacteria go into a little bit of a feeding frenzy! This provides the bacteria with the energy to multiply rapidly.

Your body's natural response to an increase in bacteria is to send white blood cells to the source of the bacteria in order to fight it and prevent any nasty infections. Once your white blood cells have killed the bacteria, they remain in your pores and are, essentially, 'dead' (pus is literally just a bunch of dead white blood cells).

Eventually, your body will absorb and break down this pus and any associated inflammation will calm down - effectively getting rid of your acne spot or pimple.

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# What Causes Acne?



## OVERPRODUCTION OF OIL

- Hormones cause oil glands to become overactive.
- Excess oil is produced.
- Oil is secreted from the pore onto the skin causing the skin to become 'greasy'.

### SOLUTION

- Skincare ingredients that reduce oil production (e.g. niacinamide, BHA, EGCG, etc.).
- Balance hormones

## BUILD UP OF DEAD SKIN CELLS

- Blocked pore prevents oil from being secreted.
- Oil becomes trapped within the pore and builds up.
- *C. acnes* bacteria feed off of trapped oil.

### SOLUTION

- Exfoliate/ increase skin cell turnover (e.g. retinoids, AHAs, BHAs, etc.)

## P-ACNES BACTERIA INCREASE

- Increase in *C. acnes* bacteria causes an immune response & inflammation.
- White blood cells sent in to fight bacteria.
- Dead white blood cells accumulate (pus).

### SOLUTION

- Reduce inflammation (e.g. antioxidants).
- Reduce bacteria (e.g. topical antibiotics, HOCl, BPO, EGCG, etc.)

## TYPES OF ACNE

There are two main types of acne: inflammatory and non-inflammatory.

Non-inflammatory acne is the initial clogged pore (officially referred to as a comedone).

When oil and dead skin cells are trapped within your pore they may be exposed to the air which causes the blockage to oxidise and turn brown/black in color. This is known as an 'open comedone' but is more frequently referred to as a blackhead.

If the blockage is not exposed to the air it is called a 'closed comedone' and more frequently referred to as a whitehead. Whiteheads often look and feel like tiny little bumps on your skin and are rarely painful.

# Types of Acne

## NON-INFLAMMATORY

## INFLAMMATORY

### Whitehead

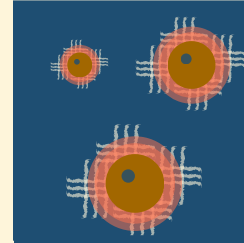
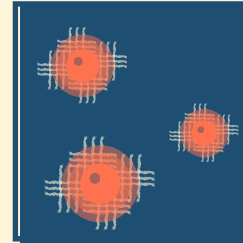
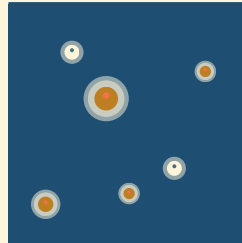
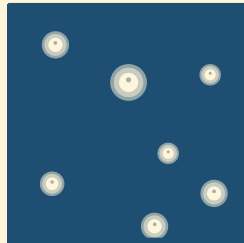
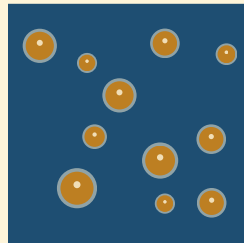
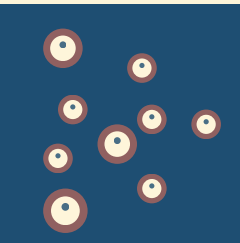
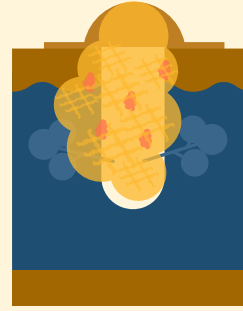
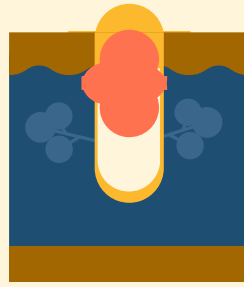
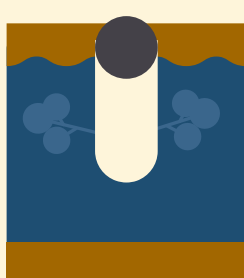
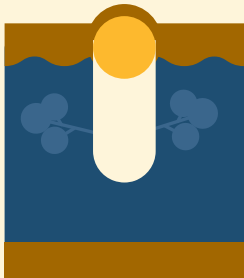
### Blackhead

### Papule

### Pustule

### Nodule

### Cyst



- Officially referred to as a closed comedone.
- Caused by dead skin cells and sebum clogging the pore.

- Officially referred to as an open comedone.
- Caused by the dead skin cells and sebum that block the pore oxidising

- A small spot that is swollen and inflamed but no pus is visible from the surface of the skin.
- Pore walls are inflamed and start to break down.

- Inflamed spot with a small amount of pus
- Has a white or yellow head.
- Pore walls break down and pore is filled with pus.

- Inflamed, large spot with or without a white/yellow head.
- Painful.
- Clog and pus are much deeper in the skin.

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### SOLUTION

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- Retinoids
- Salicylic Acid
- AHAs

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- Retinoids
- Salicylic Acid
- Benzoyl Peroxide (BPO)

- See doctor if severe
- Antibiotics
- BPO

- See dermatologist for specialist treatment.

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Treatments for non-inflammatory acne should mainly focus on increasing skin cell turnover, exfoliating skin, and reducing oil production.

As the *C. acnes* bacteria begin to multiply non-inflammatory acne can become inflammatory acne. Inflammatory acne includes papules, pustules, nodules, and cysts.

Papules are small red bumps that may or may not be painful and have no visible signs of pus.

Pustules are similar to papules but pus can be seen on the surface of the skin – these are usually the types of spots that people are tempted to pick and squeeze.

Nodules and cysts are much deeper within your skin, can be very painful, and are prone to scarring. The terms are often used interchangeably but generally speaking nodules have no visible pus, while cysts do.

Due to the increased risk of scarring, if your acne includes nodules and cysts, over-the-counter (OTC) treatments are unlikely to be very effective and you, ideally, need to see a dermatologist for more specialist treatment.

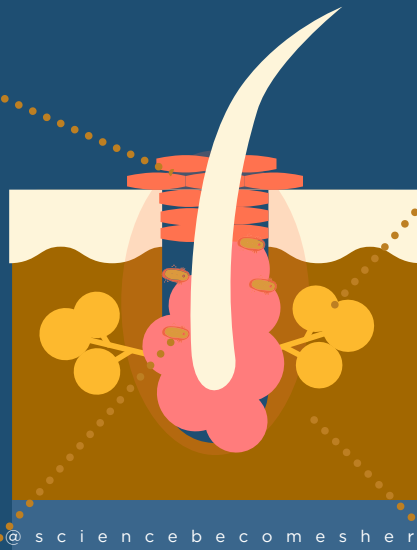
Treatments for inflammatory acne should focus on reducing the levels of bacteria and inflammation as well as increasing skin cell turnover, exfoliating, and reducing oil production.

#### DEAD SKIN CELLS

- Retinoids
- Chemical Exfoliation
  - AHAs
  - BHAs
- Physical Exfoliation
- Sulfur

#### INCREASED OIL

- Retinoids
- Niacinamide
- Green Tea
- Centella Asiatica
- Zinc
- CBD
- Eucalyptus Oil
- Clay/Charcoal



@ s c i e n c e b e c o m e s h e r

#### BACTERIA

- Benzoyl Peroxide
- Retinoids
- Niacinamide
- Green Tea
- Resveratrol
- Salicylic Acid
- Azelaic Acid
- Centella Asiatica
- CBD
- Zinc
- Sulfur
- Licorice

#### INFLAMMATION

- Retinoids
- Niacinamide
- Green Tea
- Centella Asiatica
- Resveratrol
- Aloe Vera
- Azelaic Acid
- Vitamin C
- Zinc
- Ceramides
- Licorice
- CBD

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Some research suggests that acne may also be associated with a damaged skin barrier [2], an altered skin surface pH [3], oxidative stress caused by free radicals [4], and dietary factors [5]. However, these factors affect acne by influencing hormones, oil production, bacteria, or inflammation.

In addition, genetics play a large role in the development of acne – with some research suggesting that up to 81% of the individual differences in acne are due to genetic rather than environmental factors [6]. In other words, you are more likely to get acne because your parent(s) had acne rather than because you ate too much cheese!

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## SKIN CONDITIONS THAT MAY BE MISTAKEN FOR ACNE

There are a number of skin conditions that can mimic the appearance of acne but may not respond to conventional acne treatments [7]. For this reason, if your skin is not responding to treatment, it is best to consult a dermatologist to ensure you receive an accurate diagnosis.

Common examples of skin conditions that have an acne-like appearance include:

- **Rosacea** – spots are more likely to be small, red, relatively painless, and focused around the center of your face. Your face may appear red, flushed, and you may experience broken blood vessels. The symptoms of rosacea may decrease with some acne treatments (e.g. azelaic acid) but will often return.
  - **Perioral Dermatitis** – spots are usually small, dry, itchy, and located around your mouth. It is often caused by toothpaste and the use of a barrier cream prior to brushing your teeth can help improve symptoms.
  - **Malassezia (Pityrosporum) Folliculitis (a.k.a. Fungal Acne)** – a condition that is often misdiagnosed as acne but is caused by the overgrowth of the Malassezia yeast which is present on all skin. Fungal acne is more common in males and those living in hot and humid climates. In addition, facial fungal acne is more likely to be present on your chin and the sides of your face rather than the center of your face [8].
  - **Milia** - small white bumps on your skin that are caused by a build-up of keratin under the surface of your skin. Milia are often experienced around your eye area and are unlikely to be inflamed. Newborn babies often develop milia which has led to the condition often being called ‘baby acne’ or ‘milk spots’.
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## HOW CAN ACNE BE TREATED?

Acne treatments usually focus on one or more of the underlying factors that contribute to the formation of acne. For example, acne treatments may work by:

- Regulating your hormones (e.g. oral contraceptives)
- Reducing oil production
- Increasing your rate of skin cell turnover (e.g. exfoliation)
- Controlling your *C. acnes* bacteria (e.g. antibacterials/antibiotics)
- Reducing inflammation.

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## RETINOL & OTHER RETINOLIDS

Retinoids are a catch-all term for vitamin A derivatives including; retinol, retinoic acid (tretinoin), adapalene (Differin), and retinaldehyde. While retinoic acid and adapalene are usually prescription-only treatments, retinol and retinaldehyde are available in many OTC products.

The effects of retinoid treatments are dose-dependent [9], which means that stronger products and concentrations are more effective than weaker ones. In other words, prescription treatments are going to improve acne faster than OTC products.

The main way in which retinoids work is by increasing skin cell turnover and renewal. However, they also reduce sun damage, boost collagen production, improve the appearance of wrinkles, reduce skin pigmentation, and increase skin hydration [10].

Unfortunately, due to the increase in skin cell turnover, retinoids can also cause an initial 'skin purging' by increasing the rate that blemishes are brought to the surface of your skin. They can also cause irritation, redness, dryness, and peeling during the first few weeks of use [11]. These initial side-effects are less likely with OTC forms of retinoids.

In addition to the above-mentioned skin benefits, retinoids can also reduce the inflammation that is associated with acne and acne scarring [12], and may have antioxidant [13] and antibacterial effects [14]. Specifically, retinaldehyde has demonstrated antibacterial effects against the *p-acnes* bacteria, while retinoic acid and retinol have not [14].

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*In vitro* studies (i.e. studies conducted on tissue samples) have identified that retinoids may be able to reduce oil production [15]. Unfortunately, there aren't any clinical trials that suggest this is the case. Some studies have demonstrated that retinoids can reduce pore size [16] and, as increased oil production is associated with larger pores [17], this may suggest some ability to reduce oil production.

Altogether, this suggests that retinoids can target many of the underlying causes of acne by increasing skin cell turnover, possibly reducing oil production, preventing p-acnes bacteria growth, reducing inflammation, increasing skin hydration, and by acting as an antioxidant.

Higher concentrations of retinoids have demonstrated effectiveness at treating moderate-to-severe acne [12] but there is relatively little research regarding the effectiveness of weaker forms of retinoids such as retinol. However, retinol has been observed to cause the same cellular and molecular skin changes as lower concentrations of tretinoin and is more easily absorbed into the skin [18].

Research suggests that a topical combination of retinaldehyde and glycolic acid can significantly reduce the number of acne lesions after one month of use, with continued reductions after two and three months of use [19]. In addition, this combination appears to improve acne scarring, post-inflammatory erythema (PIE), and post-inflammatory hyperpigmentation (PIH) [20].

Overall, topical retinoids have been shown to reduce the number of inflammatory and non-inflammatory acne lesions by 40-70% [21].

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## **HYDROXY ACIDS (AHA & BHA)**

There are three main types of hydroxy acids - alpha-hydroxy acids (AHAs; e.g. glycolic acid, lactic acid), beta-hydroxy acids (BHAs; e.g. salicylic acid), and polyhydroxy acids (PHAs; e.g. lactobionic acid) [22]. Hydroxy acids act as chemical exfoliants by loosening the top layer of your skin and removing dead skin cells.

Glycolic acid alone [23] as well as in combination with retinaldehyde [19] has demonstrated an ability to improve the appearance of acne and acne scarring. This is largely down to its ability to increase skin cell turnover and, thus, prevent the blocking of your pores by dead skin cells.

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In addition to increasing skin cell turnover, salicylic acid is anti-inflammatory and oil-soluble which means that it can easily penetrate your pores in order to unclog them. It does this by loosening and detaching the dead skin cells and other debris that build up within your pores [24]. Furthermore, due to its ability to dissolve in oil, salicylic acid is easily able to penetrate your oil glands and reduce oil production [25].

Salicylic acid pads were shown to reduce the number of both inflammatory and non-inflammatory acne lesions when used for 12-weeks [18]. In addition, the topical combination of salicylic acid and niacinamide is able to significantly reduce oil production and pore size after 12 weeks of use [26].

Lipohydroxy acid (LHA) is a form of salicylic acid that was developed by L'Oreal and is currently only found in their branded skincare products. Like salicylic acid, LHA dissolves in oil and is able to penetrate your oil glands. However, it does not penetrate your skin as easily, with one study finding that only 6% of LHA penetrated the skins barrier versus 58% of salicylic acid [27].

LHA is both anti-inflammatory and antibacterial [27] and has demonstrated an ability to improve acne in a number of studies [28], with one study finding that LHA was as effective at treating acne as benzoyl peroxide [29].

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## **NIACINAMIDE**

Niacinamide is a water-soluble form of vitamin B3 that can increase collagen levels, shrink pores, improve skin hydration, and reduce redness and pigmentation. In addition, it has antioxidant and anti-inflammatory effects [26], and can reduce oil production [30]. In fact, a moisturizer containing 2% niacinamide was able to reduce the rate of oil production after 2-6 weeks of use [31].

The topical application of niacinamide can lead to significant reductions in both inflammatory and non-inflammatory acne lesions when used over an 8-week period [32]. In addition, it has been shown to be more effective at improving the appearance of acne than a commonly used topical antibiotic (clindamycin) [30], although there appears to be no added benefit in using the two treatments together [33].

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## AZELAIC ACID

Azelaic acid is a naturally occurring dicarboxylic acid that is often used to treat melasma and other pigmentation disorders. It is often used to treat acne as it is both an anti-inflammatory and antimicrobial [34], and is particularly effective against the *C. acnes* bacteria [35].

Some research has found that azelaic acid is as effective as benzoyl peroxide, tretinoin, a topical antibiotic (erythromycin), and an oral antibiotic (tetracycline) at treating mild-to-moderate acne [36]. While other research found that the combination of benzoyl peroxide and a topical antibiotic (clindamycin) offered superior improvements in mild-to-moderate acne [37].

Azelaic acid may be an ideal treatment option if you experience both active acne and post-inflammatory hyperpigmentation as it is an effective ingredient for both conditions [34].

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## VITAMIN C

Vitamin C is an antioxidant that is essential for overall skin health, wound healing, and collagen production. However, only a small amount of vitamin C consumed through diet becomes available to your skin which means that topical application is required to maintain sufficient levels of vitamin C in the skin [38].

While there isn't a huge amount of research that specifically looks at how effective topical vitamin C is at treating acne, it is a potent anti-inflammatory [39] and some research suggests that blood levels of vitamin C are lower in those with acne [40].

One form of vitamin C, sodium ascorbyl phosphate (SAP), has demonstrated an ability to reduce inflammatory acne lesions by 49% after 8-weeks of use [41] and the number of acne lesions in 61-71% of individuals after 12-weeks of use [42].

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## VITAMIN E

Vitamin E is an oil-soluble antioxidant that is found at high levels in oil and oil-rich areas (e.g. the upper layers of facial skin). If too much oil is produced by the oil glands, the levels of vitamin E can decrease and lead to an increase in oxidative stress and inflammation [43].

Like vitamin C, blood levels of vitamin E have been found to be lower in those with acne, and even lower still in the case of severe acne [44]. Although there isn't much research investigating the effect of topical vitamin E on acne-prone skin, one study did find that the addition of vitamin E to a treatment regimen of benzoyl peroxide and salicylic acid reduced the number of acne lesions in as little as 2-weeks [45].

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## **GREEN TEA (EGCG)**

Topical green tea appears to have beneficial effects on a variety of skin conditions which are largely due to the antioxidant molecules (polyphenols) present in green tea. These polyphenols have demonstrated an ability to regulate inflammatory pathways in the skin [46]. The main polyphenol in green tea is EGCG (epigallocatechin-3-gallate) which seems to be responsible for green teas anti-inflammatory and antioxidant effects.

Some research has demonstrated that a topical green tea lotion can reduce oil-production by 60% after 8-weeks of use [47]. In addition, topical EGCG can improve the overall appearance of acne by reducing inflammation and inflammatory acne lesions by up to 89% and non-inflammatory acne lesions by up to 79% [48].

In other research, a green tea extract was able to reduce blackheads by 61% and pustules by 28% but had no effect on smaller non-inflammatory spots [49]. This suggests that green tea may not be an effective treatment for all types of acne.

However, as EGCG reduces inflammation, oil production, and some research suggests it prevents p-acnes bacteria growth [48], it is likely to be a good candidate for improving acne.

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## **CENTELLA ASIATICA**

Centella Asiatica (Cica) is a tropical medicinal plant that is native to Southeast Asia. It has been used for centuries to improve wound healing and treat a number of different skin conditions [50]. This is due to the composition of Cica, which contains a number of beneficial saponins (asiaticoside, Asiatic acid, madecassoside, and madasiatric acid) as well as fatty acids, flavonoids, vitamin B & C, and amino acids [51].

Some research has suggested that *Centella Asiatica* can improve overall acne severity, reduce oil production, and prevent acne-related scarring [52]. In addition, it appears to be effective at reducing certain strains of bacteria [53] and has excellent anti-inflammatory effects [54].

As mentioned earlier, acne has also been linked to reduced skin hydration, reduced antioxidant levels (especially levels of vitamin C & E), and a higher skin surface pH. The twice-daily application of a *Centella Asiatica* extract has demonstrated an ability to increase skin hydration and reduce the skin's pH level [55], as well as increase the levels of antioxidants in the skin. Specifically, the extract was able to increase vitamin C levels by 36% and vitamin E levels by 77% after 7-days of use [56].

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## TEA TREE OIL

Tea tree oil has been used medicinally for decades due to its antibacterial and antifungal properties [57]. In addition, research suggests that tea tree oil acts as an anti-inflammatory [58].

In one study, a 5% tea tree oil gel was 3.5 times more effective at reducing the total number of acne lesions and 5.75 times more effective at reducing overall acne severity than a placebo over a 6-week period [59]. In fact, tea tree oil has demonstrated a similar effectiveness to benzoyl peroxide for the treatment of acne but takes longer to see results [60].

Other research found that a topical combination of tea tree oil, propolis, and aloe vera was more effective at reducing the number of acne lesions, as well as the overall severity of acne and red scarring than a commonly used antibiotic cream [61].

A downside to the use of tea tree oil for acne is that it can cause skin irritation and allergic reactions. However, the research appears to be conflicting regarding this [62].

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## OTHER POTENTIAL ACNE TREATMENTS

A number of ingredients possess one or more qualities that would suggest they are beneficial in the treatment of acne. For example, by reducing inflammation, preventing *C. acnes* bacteria growth, reducing oil production, or increasing skin cell turnover. However, they are yet to be fully investigated in clinical trials, and any research to support their anti-acne effects is so-far lacking.

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### SNAIL MUCIN

Snail mucin (otherwise known as 'snail slime' or snail secretion filtrate) is an animal-derived growth factor that can help encourage wound-healing [63]. This is down to the chemicals that can be found in snail mucin, including allantoin, glycolic acid, hyaluronic acid, natural antibacterials, collagen, and elastin [64].

This mix of chemicals would suggest that snail mucin may be beneficial if you have acne, particularly as it promotes wound healing and reduces bacterial activity. There is plenty of anecdotal evidence available online to suggest that snail mucin has improved the appearance of acne for some people. However, so far, no research exists to support these claims.

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### RESVERATROL

Resveratrol is an antioxidant that has anti-inflammatory and wound-healing effects [65], more recent research has identified that it is also effective at preventing the growth of the *C. acnes* bacteria [66]. A pilot study identified that resveratrol was able to reduce the severity of acne and the size of acne lesions but suggested that more research was needed to determine whether resveratrol is an effective treatment for acne [67].

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### ZINC

Various forms of zinc have also been identified as useful acne treatments, although there is stronger evidence to support the use of oral zinc rather than topical zinc [18]. One study found that the topical application of zinc improved the appearance of acne but these results were not statistically significant [68]. However, zinc does seem to be effective when combined with a topical antibiotic (erythromycin) [69].

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## **SULFUR**

Sulfur is a non-metallic natural element that has been used for hundreds of years to treat acne due to its antibacterial properties. It is also thought to increase skin cell turnover and is usually combined with an ingredient called resorcinol. Resorcinol is another antibacterial ingredient that can increase skin cell turnover and the two together can often cause mild irritation and sensitisation. However, sulfur products aren't usually that popular because they often smell particularly bad [18].

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## **CERAMIDES**

As mentioned earlier, dehydrated skin due to a damaged skin barrier can indirectly cause acne by increasing oil production and inflammation. Research suggests that the skin of individuals with acne also has a reduced amount of ceramides compared to those without acne [70]. The application of ceramides to the skin has both a hydrating and anti-inflammatory effect [71], which may be beneficial if you have acne.

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## **ALOE VERA**

Aloe Vera contains a number of active components such as vitamins A, C, and E, zinc, saponins, salicylic acids, and amino acids. It is these components that are largely responsible for Aloe's healing, anti-inflammatory, hydrating, and antiseptic effects [72] and may make it an effective acne treatment.

As mentioned earlier, when combined with tea tree oil and propolis, aloe vera was more effective at reducing the number of acne lesions, as well as the overall severity of acne, than a commonly used antibiotic cream [61].

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## **WITCH HAZEL**

Witch Hazel is a commonly used astringent that can help cleanse your skin, dry out oil, and reduce pore size, and has antioxidant, anti-inflammatory, and antiseptic properties [73]. However, it may be excessively drying which may worsen acne if your skin barrier function is reduced.

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## **EUCALYPTUS OIL**

Eucalyptus oil is extracted from the Australian Eucalyptus plant and has been used medicinally by Australia's Aboriginal population for thousands of years due to its anti-inflammatory and antibacterial properties [74]. More recently, research has demonstrated that eucalyptus oil is particularly effective against the *C. acnes* bacteria [75] and can shrink the size of oil glands, thus reducing oil production [76].

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## **CLAY MINERALS & ACTIVATED CHARCOAL**

Clay minerals (e.g. kaolin, bentonite) are very good at absorbing oils, impurities, toxins, and other contaminants from your skin. This helps to cleanse and refresh skin and heal blemishes [77]. In addition, clay minerals have demonstrated antibacterial activity against a number of different antibiotic-resistant bacteria [78].

Activated charcoal is thought to absorb oils and toxins in a similar way to clay minerals but there is limited research surrounding its use in skincare. However, charcoal is often used in medical cases of poisoning due to its ability to absorb toxins in your body [79]. In addition, it may have antibacterial properties.

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## **LICORICE**

Licorice root extract is widely used for reducing pigmentation, brightening skin, and reducing the signs of aging. It contains a variety of substances including flavonoids, saponins, amino acids, and sterols but its effectiveness as a skin treatment is largely down to an ingredient called glycyrrhizin [80]. Glycyrrhizin has both antioxidant [81] and anti-inflammatory [82] properties which suggest that it may be a suitable acne treatment. In addition, other research has demonstrated that licorice extracts demonstrate antibacterial activity against the *C. acnes* bacteria [83].

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## **SELECTING ACNE TREATMENTS**

In terms of selecting treatments to improve acne, you should ensure that the four main bases are covered – a treatment that reduces oil production, a treatment that increases skin cell turnover, a treatment that reduces bacteria, and a treatment that reduces inflammation.

In addition, including an antioxidant and an ingredient that increases skin hydration may further improve acne.

For example, the combination of salicylic acid and niacinamide covers all of the four main bases and the additional two mentioned above. Both salicylic acid and niacinamide reduce oil production and inflammation and salicylic acid increases skin cell turnover and fights bacteria. Niacinamide is also a potent antioxidant that can improve skin hydration by increasing the level of ceramides within the skin.

These ingredients could be applied in the treatment step of your skincare routine or by selecting a salicylic-acid-containing cleanser and a moisturiser with niacinamide.

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# Acne Ingredient Cheat Sheet

There are four main factors that overlap to cause acne. These are excessive oil production, the build-up of dead skin cells on the surface of the skin, a bacteria known as *C. acnes*, inflammation as part of an immune response to the bacteria.

Research also suggests that those with acne may have reduced levels of hydration and antioxidants within the skin.

INGREDIENT	REDUCES OIL PRODUCTION	ANTI-BACTERIAL	ANTI-INFLAMMATORY	INCREASES SKIN CELL TURNOVER	BONUS	
					HYDRATES	ANTI-OXIDANT
Retinoids		✓	✓	✓	✓	✓
AHA				✓	✓	
BHA	✓	✓	✓	✓		
Niacinamide	✓		✓		✓	✓
Azelaic Acid		✓	✓			
Vitamin C			✓		✓	✓
Vitamin E			✓		✓	✓
Green Tea	✓	✓	✓			✓
Centella	✓	✓	✓		✓	✓
Tea Tree Oil		✓	✓			
Snail Mucin		✓	✓		✓	
Resveratrol		✓	✓			✓
Zinc	✓	✓	✓			
Sulfur		✓		✓		
Ceramides			✓		✓	
Aloe		✓	✓		✓	✓
Witch Hazel	✓	✓	✓			✓
Eucalyptus Oil	✓	✓	✓			
Clay/Charcoal	✓	✓				
Licorice		✓	✓			✓

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## NON-TREATMENT TIPS FOR DEALING WITH ACNE

The most important non-treatment tip for dealing with acne is to **be kind to yourself**. Individuals with acne report greater emotional distress, anxiety, and depression than those with a number of other medical conditions, including cancer [84]. While effective treatment can improve self-esteem, body image, and self-confidence [85], it usually takes time to see results and is an ongoing process.

In addition, treatments that increase skin cell turnover can initially make acne appear worse by causing skin purging which can last for weeks or months depending on the strength of the treatment.

If you are experiencing emotional distress as a result of acne (or for any other reason) and it's impacting your quality of life, please seek the help of an appropriate medical professional.

Unfortunately, there are a lot of misinformed people who will try to offer unsolicited advice and make you feel like acne is due to poor hygiene, poor diet, or overall poor health. However, this is not the case.

While there are a number of lifestyle factors that may indirectly contribute to the development of acne, they do so by affecting either hormones, oil production, dead skin cell build-up (or clogged pores), the p-acnes bacteria, and inflammation - all biological factors that are largely determined by your genetics rather than your lifestyle.

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## DIET

Over the past decade or so, there has often been speculation about whether or not certain dietary factors cause acne. Most of this speculation revolved around chocolate and dairy products but the evidence so far has been limited.

For example, dermatologists and patients report an increase in breakouts after consuming chocolate but the research appears to be inconclusive, with the majority of studies finding no relationship between chocolate and acne [86].

This may be due to the additional ingredients found in the chocolate bars and the control bars (used as a comparison) used in the research studies, such as milk and sugar, and the fact that they have a high glycaemic index (GI).

A diet rich in high GI products can increase the levels of insulin in your blood. Higher insulin levels then stimulate androgen hormones which increase the production of oil in your skin. This means that diet may indirectly cause acne via its effect on insulin metabolism [87].

In fact, research has found that a low GI diet reduced the severity of acne and improved insulin sensitivity in young men with acne [88].

Dairy products are low GI foods but contain hormones that are produced by the cows during pregnancy, including insulin-like growth factor 1 (IGF-1) – a hormone that increases oil production. Levels of IGF-1 appear to be higher in those with acne than in those without and are positively correlated with acne severity [89]. This means that the more severe a person's acne is, the higher their blood levels of IGF-1.

This would suggest that, in theory, dairy products may cause acne or worsen existing acne. However, it appears that only certain types of dairy are an issue. For example, in one study, acne was associated with increased consumption of milk and ice cream but not yogurt, cheese, or chocolate [90].

Other research has found positive correlations between acne and cottage cheese, cream cheese, instant breakfast drinks that contained dairy, and milk – particularly low-fat (skimmed) milk [91]. Another study found a link between acne and skimmed milk but not whole (full-fat) milk [92].

Altogether, this research would suggest that acne may be associated with milk, particularly skimmed milk, but not with other dairy products [86].

Not only are those with acne more likely to report higher levels of depression and anxiety than those without, but they are also more likely to experience gastrointestinal distress (e.g. constipation, acid reflux, etc.). In addition, they are 37% more likely to experience abdominal bloating [93].

One factor that has been linked to mental health, gastrointestinal distress, and inflammatory skin disorders, such as acne, is the gut microbiome [94]. The theory behind this focuses on how emotional states, such as worry, depression, and anxiety, may alter your gut microbiome and, as a consequence, lead to increased inflammation [95].

Although the research regarding acne and the gut microbiome is limited, other inflammatory skin conditions, such as acne rosacea, have been linked to a ten-fold increase in small intestine bacterial overgrowth compared to those without skin inflammation [96]. This means that they had ten times the amount of bacterial overgrowth than was considered 'normal.'

Furthermore, when this bacterial overgrowth was treated (i.e. medication was used to return it to 'normal' levels), inflammatory skin lesions cleared almost completely. Interestingly, oral probiotics can reduce this bacterial overgrowth in a similar way [97]. This research focused on treating irritable bowel syndrome (IBS) with a well-known probiotic drink (Yakult) but, if the gut microbiome theory of inflammatory skin conditions is correct, it begs the question as to whether oral probiotics may improve acne.

The take-home message here is that there isn't a huge amount of evidence to support the role of diet in acne. The strongest evidence appears to be for high GI foods as they alter hormones and, as a consequence, increase oil production. Dairy consumption has long been suggested as a cause of acne, however, the evidence for this is fairly weak (with the exception of skimmed milk). An altered gut microbiome may play a role in acne by increasing inflammation but so far this appears to be based on theory rather than research.

Either way, you might find that the following diet-based tips may improve acne:

- Basing your diet around low GI foods and avoiding sugar and other foods that may spike insulin levels.
- Choosing whole-fat milk over skimmed milk or avoiding milk altogether.
- Including probiotics in your diet.

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## **STRESS**

Research has demonstrated that stress levels are positively correlated with acne severity [98] - meaning that the higher a person's stress level is, the more severe their acne is likely to be.

When the brain senses stress, a hormone called corticotropin-releasing hormone (CRH) is secreted which begins a process that results in the production of cortisol (the main stress hormone in humans) [99].

CRH has also been found to increase oil production [100] and inflammation [101] which may explain the association between stress and acne. However, some research found that, although stress was associated with more severe acne, it was not associated with increased oil production [102].

As mentioned earlier, another way that stress may increase inflammation, and thus acne severity, may be through alterations to the gut microbiome.

Overall, there appears to be a link between stress and acne, although it is not quite clear what causes this association. Nevertheless, reducing stress may help improve acne.

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## **HAND HYGIENE & OBJECTS THAT COME INTO CONTACT WITH YOUR FACE**

As mentioned earlier, acne is not due to poor hygiene regardless of what misinformed people may tell you. There are, however, certain aspects of hygiene that may contribute to acne - namely touching your face with your hands or other objects.

This is because your hands come into contact with so many different types of bacteria and environmental pollutants on a daily basis. What's more, you then transfer all this debris onto your phone.

In fact, throughout the day, it won't just be bacteria and environmental pollutants that build up on your phone, but also facial oil and make-up. Each time you make or receive a phone call, you then transfer this bacteria and debris to your facial skin which can then contribute to acne by clogging your pores.

There isn't actually any research to suggest that mobile phones contribute to acne and, considering that approximately 70 - 95% of the general population are right-handed, 68% of which are more likely to hold their phone to their right ear [103], you would think that research would have identified an increased incidence/severity of acne on the right side of the face.

What research does tell us though, is that our mobile phones are definitely a wild breeding ground for bacteria [104].

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In any case, if you are experiencing acne on one side of your face more than the other, you may want to make sure you are regularly cleaning your phone. Another reason for asymmetrical acne may be due to dirty pillowcases. This is because you transfer any dirt, oil, bacteria, and other debris from your face to your pillow when you sleep, and, after a while, it will build up.

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To reduce the risk of the above factors contributing to acne, here are some take-away tips:

- Clean your phone regularly – as often as is convenient but ideally before you make or receive a phone call.
  - Change your pillowcases regularly – ideally at least once-a-week.
  - Avoid resting your head in your hands or touching your face too often.
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# MICROCOMEDONES & THE IMPORTANCE OF MAINTENANCE ACNE TREATMENT

Microcomedones (sometimes referred to as subclinical acne) are tiny little pouches within your pores that are filled with oil, bacteria, and dead skin cells. They are invisible to your naked eye but will eventually turn into clogged pores if they fill-up too much [105].

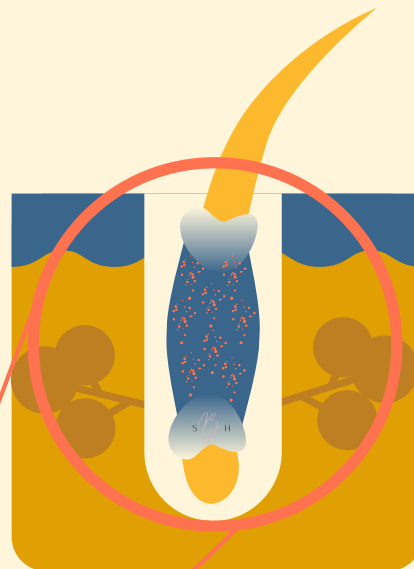
It is estimated that, if you have acne-prone skin, up to 30% of your pores in any area of visibly clear skin may contain microcomedones. In comparison, only 0.25% of pores on your entire face are involved in visible acne - even in fairly severe cases [106].

For this reason, it's important to continue acne treatments even when your skin is visibly clear.

## Microcomedones

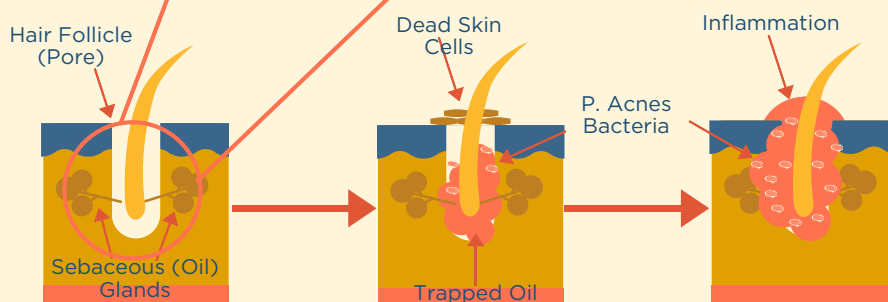
### WHAT IS IT?

- Acne that is not visible on the surface of your skin (sometimes referred to as 'subclinical acne'.)
- Described as a 'specialised skin compartment where acne arises'.
- May be present in up to 30% of pores on the visibly clear skin of individuals prone to acne.
- At a microscopic level it looks like a tiny little pouch filled with oil, bacteria, and dead skin cells.



### HOW TO TREAT

- Treatment mainly involves preventing the microcomedone from completely blocking the pore and becoming active acne.
- Apply acne treatments to all skin rather than just to the active acne.
- Using retinoids to increase skin cell turnover.
- Using chemical exfoliants such as AHAs to help exfoliate the top layer of skin and BHAs to exfoliate within the pore.



Adapted from a microscopic image of a microcomedone in: Josse, G. et al. (2019). 'High Bacterial Colonization and Lipase Activity in Microcomedones', *Exp Dermatol.*, 29(2), pp. 168-176.

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## SOURCES & FURTHER READING

1. Jacob, C., Dover, J. & Kaminer, M. (2001). 'Acne scarring: a classification system and review of treatment options', *J Am Acad Dermatol.*, 45(1), pp. 109-117.
  2. Yamamoto, A., Takenouchi, K. & Ito, M. (1995). 'Impaired water barrier function in acne vulgaris', *Arch Dermatol Res.*, 287(2), pp. 214-218.
  3. Prakash, C., Bhargava, P., Tiwari, S., Majumdar, B. & Bhargava, R. (2017). 'Skin surface pH in acne vulgaris: insights from an observational study and review of the literature', *J Clin Aesthet Dermatol.*, 10(7), pp. 33-39.
  4. Mills, O., Criscito, M., Schlesinger, J., Verdicchio, R. & Szoke, E. (2016). 'Addressing free radical oxidation in acne vulgaris', *J Clin Aesthet Dermatol.*, 9(1), pp. 25-30.
  5. Kucharska, A., Szmurlo, A. & Sinska, B. (2016). 'Significance of diet in treated and untreated acne vulgaris', *Postepy Dermatol Alergol.*, 33(2), pp. 81-86.
  6. Bataille, V., Snieder, H., MacGregor, A., Sasieni, P., & Spector, T. (2002). 'The influence of genetics and environmental factors in the pathogenesis of acne: a twin study of acne in women'. *Journal of Investigative Dermatology*, 119, pp. 317-322.
  7. Al-Natour, S. (2012). 'Acne mimickers: Another cause for unresponsive acne', *Journal of The Saudi Society of Dermatology & Dermatologic Surgery*, 16(2), pp. 35-40.
  8. Rubenstein, R. & Malerich, S. (2014). 'Malassezia (Pityrosporum) Folliculitis', *J Clin Aesthet Dermatol.*, 7(3), pp. 37-41.
  9. Leyden, J., Stein-Gold, L. & Weiss, J. (2017). 'Why topical retinoids are the mainstay therapy for acne', *Dermatol Ther.*, 7(3), pp. 293-304.
  10. Mukherjee, S., Date, A., Patravale, V. et al. (2006). 'Retinoids in the treatment of skin aging: an overview of clinical efficacy and safety', *Clin Interv Aging*, 1, pp. 327-348.
  11. Song, X., Xu, A., Pan, W. et al. (2008). 'Nicotinamide attenuates aquaporin 3 overexpression induced by retinoic acid through inhibition of EGFR/ERK in cultured human skin keratinocytes', *Int J Mol Med.*, 22(2), pp. 1107-1175.
  12. Tan, J., Tanghetti, E., Baldwin, H., Stein Gold, L. & Lain, E. (2019). 'The role of topical retinoids in the prevention and treatment of atrophic acne scarring: Understanding the importance of early effective treatment', *J Drugs Dermatol.*, 18(3), pp. 255-260.
  13. Sorg, O., Tran, C. & Saurat, J. (2001). 'Cutaneous vitamins A and E in the context of ultraviolet- or chemically-induced oxidative stress', *Skin Pharmacol Appl Skin Physiol.*, 14, pp. 363-372.
  14. Pechere, M., Germainier, L., Siegenthaler, G., Pechere, J. & Saurat, J. (2002). 'The antibacterial activity of topical retinoids: the case of retinaldehyde', *Dermatology*, 205(2), pp. 153-158.
  15. Zouboulis, C., Korge, B., Akamatsu, H., Xia, L., Schiller, S., Gollnick, H. & Orfanos, C. (1991). 'Effects of 13-cis-retinoic acid, all-trans-retinoic acid, and acitretin on the proliferation, lipid synthesis and keratin expression of cultured human sebocytes in vitro', *J Invest Dermatol.*, 96(5), pp. 792-797.
  16. Bouloc, A., Verganini, A. & Issa, M. (2015). 'A double-blind randomized study comparing the association of retinol and LR2412 with tretinoin 0.025% in photoaged skin', *J Cosmet Dermatol*, 14, pp. 40-46.
  17. Lee, S., Seok, J., Jeong, S., Park, K., Li, K. & Seo, S. (2016). 'Facial pores: definition, causes, and treatment options', *Dermatologic Surg.*, 42(3), pp. 277-285.
  18. Decker, A. & Graber, E. (2012). 'Over-the-counter acne treatments - A review', *J Clin Aesthet Dermatol.*, 5(5), pp. 32-40.
  19. Poli, F., Ribet, V., Lauze, C., Adhoute, H. & Morinet, P. (2005). 'Efficacy and safety of 0.1% retinaldehyde/ 6% glycolic acid (Diacneal) for mild to moderate acne vulgaris', *Dermatology*, 210(Suppl 1), pp. 14-21.
  20. Katsambas, A. (2005). 'RALGA (Diacneal), a retinaldehyde and glycolic acid association and post-inflammatory hyperpigmentation in acne - a review', *Dermatology*, 210(Suppl 1), pp. 39-45.
  21. Halder, A. & Shaw, J. (2004). 'Treatment of acne vulgaris', *JAMA*, 292(6), pp. 726-735.
  22. Kornhauser, A., Coelho, S. & Hearing, V. (2010). 'Applications of hydroxy acids: classification, mechanisms, and photoactivity', *Clin Cosmet Investig Dermatol*, 3, pp.135-142.
  23. Wang, C., Huang, C., Hu, C. & Chan, H. (1997). 'The effect of glycolic acid on the treatment of acne in Asian skin', *Dermatologic Surg*, 23(1), pp. 23-29.
  24. Davies, M. & Marks, R. (1976). 'Studies on the effect of salicylic acid on normal skin', *Br J Dermatol.*, 95(2), pp. 187-192.
  25. Marczyk, B., Mucha, P., Budzisz, E., Rotsztein, H. (2014). 'Comparative study of the effect of 50% pyruvic and 30% salicylic peels on the skin lipid film in patients with acne vulgaris', *J Cosmet Dermatol*, 13(1), pp. 15-21.
  26. Berson, D., Osborne, R., Oblong, J., Hakozaki, T., Jonson, M. & Bissett, D. (2014). 'Chapter 10: Niacinamide: A topical vitamin with wide-ranging skin appearance benefits', *Cosmeceuticals and Cosmetic Practice: First Edn.* John Wiley & Sons Ltd.
  27. Saint-Leger, D., Leveque, J. & Verschoore, M. (2007). 'The use of hydroxy acids on the skin: characteristics of C8-lipo hydroxy acid', *J Cosmet Dermatol.*, 6(1), pp. 59-65.
  28. Zeichner, J. (2016). 'The use of lipo hydroxy acid in skincare and acne treatment', *J Clin Aesthet Dermatol.*, 9(11), pp. 40-43.
  29. Bissonnette, R., Bolduc, C., Seite, S., Nigen, S., Provost, N., Maari, C. & Rougier, A. (2009). 'Randomized study comparing the efficacy and tolerance of a lipophilic hydroxy acid derivative of salicylic acid and 5% benzoyl peroxide', *J Cosmet Dermatol.*, 8(1), pp. 19-23.
  30. Shalita, A., Smith, J., Parish, L., Sofman, M. & Chalker, S. (1995). 'Topical nicotinamide compared with clindamycin gel in the treatment of inflammatory acne vulgaris. *International Journal of Dermatology*, 34, pp.434-437.
  31. Draelos, Z., Matsubara, A. & Smiles, K. (2006). 'The effect of 2% niacinamide on facial sebum production'. *Journal of Cosmetic Laser Therapy*, 8, pp.96-101.
  32. Kaymak, Y. & Onder, M. (2008). 'An investigation of the efficacy of topical niacinamide for the treatment of mild to moderate acne vulgaris'. *Journal of the Turkish Academy of Dermatologists*, 2(4).
  33. Sardesai, V. & Kambli, V. (2003). 'Comparison of efficacy of topical clindamycin and nicotinamide combination with plain clindamycin for the treatment of acne vulgaris and acne resistant to topical antibiotics', *Indian J Dermatol Venereol Leprol.*, 69(2), pp. 138-139.
  34. Canavan, T., Chen, E. & Elewski, B. (2016). 'Optimizing non-antibiotic treatments for patients with acne: a review', *Dermatol Ther.*, 6(4), pp. 555-578.
  35. Sieber, M. & Hegel, J. (2014). 'Azelaic acid: Properties and mode of action', *Skin Pharmacol Physiol.*, 27(Suppl 1), pp. 9-17.
  36. Fitton, A. & Goa, K. (1991). 'Azelaic acid. A review of its pharmacological properties and therapeutic efficacy in acne and hyperpigmentary disorders', *Drugs*, 41(5), pp. 780-798.
  37. Schaller, M., Sebastian, M., Röss, C., Seidel, D. & Hennig, M. (2016). 'A multicentre, randomized, single-blind, parallel-group study comparing the efficacy and tolerability of benzoyl peroxide 3%/clindamycin 1% with azelaic acid 20% in the topical treatment of mild-to-moderate acne vulgaris', *J Eur Acad Dermatol Venereol.*, 30(6), pp. 966-973.
-



38. Al-Niaimi, F. & Chiang, N. (2017). 'Topical vitamin C and the skin: mechanisms of action and clinical applications', *J Clin Aesthet Dermatol*, 10(7), pp. 14-17.
39. Farris, P. (2006). 'Topical vitamin C: A useful agent for treating photoaging and other dermatologic conditions', *Dermatol Surg*, 31, pp. 814-818.
40. Abuldnaja, K. (2009). 'Oxidant/antioxidant status in obese adolescent females with acne vulgaris', *Indian J Dermatol*, 54(1), pp. 36-40.
41. Ruamrak, C., Lourith, N. & Natakankitkul, S. (2009). 'Comparison of clinical efficacies of sodium ascorbyl phosphate, retinol, and their combination in acne treatment', *Int J Cosmet Sci*, 31(1), pp. 41-46.
42. Woolery-Lloyd, H., Baumann, L. & Ikeno, H. (2010). 'Sodium L-ascorbyl-2-phosphate 5% lotion for the treatment of acne vulgaris: a randomized, double-blind, controlled trial', *J Cosmet Dermatol*, 9(1), pp. 22-27.
43. Thiele, J., Weber, S. & Packer, L. (1999). 'Sebaceous gland secretion is a major physiologic route of vitamin E delivery to skin', *J Invest Dermatol*, 113(6), pp. 1006-1010.
44. Ozuguz, P., Dogruk Kacar, S., Ekiz, O., Takci, Z., Balta, I. & Kalkan, G. (2014). 'Evaluation of serum vitamins A and E and Zinc levels according to the severity of acne vulgaris', *Cutan Ocul Toxicol*, 33(2), pp. 99-102.
45. Mills, O., Criscione, M., Schlesinger, J., Verdicchio, R. & Szoke, E. (2016). 'Addressing free radical oxidation in acne vulgaris', *J Clin Aesthet Dermatol*, 9(1), pp. 25-30.
46. Katiyar, S. & Elmets, C. (2001). 'Green tea polyphenolic antioxidants and skin photoprotection (Review)', *Int J Oncol*, 18, pp. 1307-1313.
47. Mahmood, T., Akhtar, N., Khan, B. & Saeed, T. (2010). 'Outcomes of 3% green tea emulsion on skin sebum production in male volunteers', *Bosn J Basic Med. Sci.*, 10(3), pp. 260-264.
48. Yoon, J., Kwon, H., Min, S., Thiboutot, D. & Suh, D. (2013). 'Epigallocatechin-3-gallate improves acne in humans by modulating intracellular molecular targets and inhibiting P.acnes', *J Invest Dermatol*, 133(2), pp. 429-440.
49. Jung, M., Ha, S., Song, J., Song, J., Houh, Y., Cho, E., Chun, J., Yoon, S., Yang, Y., Bang, S., Kim, M., Park, H. & Cho, D. (2012). 'Polyphenol-60 displays a therapeutic effect on acne by suppression of TLR2 and IL-8 expression via down-regulating the ERK1/2 pathway'. *Arch Dermatol Res*, 304(8), pp. 655-663.
50. Gohil, K., Patel, J. & Gajjar, A. (2010). 'Pharmacological Review on Centella Asiatica: A potential herbal cure-all', *Indian J Pharm Sci*, 72(5), pp. 546-556.
51. Singh, S., Gautam, A., Sharma, A. & Batra, A. (2010). 'Centella Asiatica: A plant with immense medicinal potential but threatened', *Int J Pharm Sci Rev Res*, 4(2), pp. 9-17.
52. Beltrami, B., Vassallo, C., Berardesca, E. & Borroni, G. (2001). 'Anti-inflammatory, antimicrobial, comedolytic effects of a topical plant complex treatment in acne vulgaris: A clinical trial', *J Appl Cosmetol*, 19, pp. 11-20.
53. Nasution, Y., Restuati, M., Pulungan, A., Pratiwi, N. & Dinningrat, D. (2018). 'Antimicrobial activities of Centella Asiatica leaf and root extracts on selected pathogenic micro-organisms', *J Med Sci*, 18, pp. 198-204.
54. Ho, J., Sung, J., Cheon, K. & Tae, J. (2018). 'Anti-inflammatory effect of Centella Asiatica phytosome in a mouse model of phthalic anhydride-induced atopic dermatitis', *Phytomedicine*, 43, pp. 110-119.
55. Ratz-Lyko, A., Arct, J. & Pytkowska, K. (2016). 'Moisturizing and anti-inflammatory properties of cosmetic formulations containing Centella Asiatica extract', *Indian J Pharm Sci*, 78(1), pp. 27-33.
56. Shukla, A., Rasik, A. & Dhawan, B. (1999). 'Asiaticoside-induced elevation of antioxidant levels in healing wounds', *Phytother Res*, 13(1), pp. 50-54.
57. Cox, S., Mann, C., Markham, J., Bell, H., Gustafson, J., Warmington, J. & Willey, S. (2000). 'The mode of antimicrobial action of the essential oil of Melaleuca alternifolia (tea tree oil)', *J Appl Microbiol*, 88(1), pp. 170-175.
58. Hart, P., Brand, C., Carson, C., Riley, T., Prager, R. & Finlay-Jones, J. (2000). 'Terpinen-4-ol, the main component of essential oil of Melaleuca alternifolia (tea tree oil), suppresses inflammatory mediator production by activated human monocytes', *Inflamm Res*, 49(11), pp. 619-626.
59. Enshaieh, S., Jooya, A., Siadat, A., Iraj, F. (2007). 'The efficacy of 5% topical tea tree oil gel in mild to moderate acne vulgaris: a randomized, double-blind placebo-controlled study', *Indian J Dermatol Venereol Leprol*, 73(1), pp. 22-25.
60. Bassett, I., Pannowitz, D. & Barnetson, R. (1990). 'A comparative study of tea-tree oil versus benzoyl peroxide in the treatment of acne', *Med J Aust*, 153(8), pp. 455-458.
61. Mazzaello, V., Donadu, M., Ferrari, M., Piga, G., Usai, D., Zanetti, S. & Sotgiu, M. (2018). 'Treatment of acne with a combination of propolis, tea tree oil, and aloe vera compared to erythromycin cream: two double-blind investigations', *Clin Pharmacol*, 10, pp. 175-181.
62. Carson, C., Hammer, K. & Riley, T. (2006). 'Melaleuca alternifolia (Tea Tree) Oil: a review of antimicrobial and other medicinal properties', *Clin Microbiol Rev*, 19(1), pp. 50-62.
63. Bucay, V. & Day, D. (2013). 'Adjunctive Skin Care of the Brow and Periorbital Region', *Clin Plastic Surg*, 40, pp. 225-236.
64. Gonzalez, M., Egana, M. & Munoz, N. (2004). 'Crema de caracol para tratamiento coayudante de cicatrices de quemaduras e injertos', *Revisita Chilena de Terapia Ocupacional*, 4, pp. 5-10.
65. Baur, J. & Sinclair, D. (2006). 'Therapeutic potential of resveratrol: the in vivo evidence', *Nat Rev Drug Discov*, 5(6), pp. 493-506.
66. Taylor, E., Yang, Y., Champer, J. & Kim, J. (2014). 'Resveratrol demonstrates antimicrobial effects against propionibacterium acnes in vitro', *Dermatol Ther*, 4(2), pp. 249-257.
67. Fabbrocini, G., Staibano, S., De Rosa, G. et al. (2011). 'Resveratrol-containing gel for the treatment of acne vulgaris: a single-blind, vehicle-controlled, pilot study', *Am J Clin Dermatol*, 12(2), pp. 133-141.
68. Sharquie, K., Noaimi, A. & Al-Salih, M. (2008). 'Topical therapy of acne vulgaris using 2% tea lotion in comparison with 5% zinc sulfate solution', *Saudi Med J*, 29(12), pp. 1757-1761.
69. Langner, A., Sheehan-Dare, R., Layton, A. (2007). 'A randomized, single-blind comparison of topical clindamycin + benzoyl peroxide (Duac) and erythromycin + zinc acetate (Zineryt) in the treatment of mild to moderate facial acne vulgaris', *J Eur Acad Dermatol Venereol*, 21(3), pp. 311-319.
70. Yamamoto, A., Takenouchi, K. & Ito, M. (1995). 'Impaired water barrier function in acne vulgaris', *Arch Dermatol Res*, 287(2), pp. 214-218.
71. Carneiro, R., Salgado, A., Raposo, S., Marto, J., Simoes, S., Urbano, M. & Ribeiro, H. (2011). 'Topical emulsions containing ceramides: Effects on the skin barrier function and anti-inflammatory properties', *Eur J Lipid Sci*, 113(8), pp. 961-966.
72. Surjushe, A., Vasani, R. & Saple, D. (2008). 'Aloe Vera: A short review', *Indian J Dermatol*, 53(4), pp. 163-166.
73. Thring, T., Hill, P. & Naughton, D. (2011). 'Antioxidant and potential anti-inflammatory activity of extracts and formulations of white tea, rose, and witch hazel on primary human dermal fibroblast cells', *J Inflamm*, 8, pp. 27.
74. Dodov, M. & Kulevanova, S. (2009). 'A review of phytotherapy of acne vulgaris', *Macedonian Pharmaceutical Bulletin*, 55(1-2), pp. 3-22.
75. Athikomkulchai, S., Watthanachaiyingcharoen, R., Tunvichien, S. et al. (2008). 'The development of anti-acne products from eucalyptus globulus and psidium guajava oil', *J Health Res*, 22(3), pp. 109-113.
76. Bhatt, D., Sachan, A., Jain, S. & Barik, R. (2011). 'Studies on the inhibitory effect of Eucalyptus oil on sebaceous glands for the management of acne', *Indian J Natural Products and Resources*, 2(3), pp. 345-349.
77. Williams, L. & Haydel, S. (2010). 'Evaluation of the medicinal use of clay minerals as antibacterial agents', *Int Geol Rev*, 52(7/8), pp. 745-770.
78. Haydel, S., Remenih, C. & Williams, L. (2008). 'Broad-spectrum in vitro antibacterial activities of clay minerals against antibiotic-susceptible and antibiotic-resistant bacterial pathogens', *J Antimicrob Chemother*, 61(2), pp. 353-361.

- 
79. Villarreal, J., Kahn, C., Dunford, J., Patel, E. & Clark, R. (2015). 'A retrospective review of the prehospital use of activated charcoal', *Am J Emerg Med.*, 33(1), pp. 56-59.
80. Karaogul, E., Parlar, P., Parlar, H. & Alma, M. (2016). 'Enrichment of the glycyrrhizic acid from licorice roots (*Glycyrrhiza glabra* L.) by isoelectric focused adsorptive bubble chromatography', *J Analytical Methods Chem.*, Article ID 7201740, 5 pages.
81. Ju, H., Li, X., Zhao, B., Han, Z. & Xin, W. (1989). 'Effects of glycyrrhiza flavonoid on lipid peroxidation and active oxygen radicals', *Acta Pharmaceutica Sinica*, 24(11), pp. 807-812.
82. Yokota, T., Nishio, H., Kubota, Y. & Mizoguchi, M. (1998). 'The inhibitory effect of glabridin from licorice extracts on melanogenesis and inflammation', *Pigment Cell Research*, 11(6), pp. 355-361.
83. Nam, C., Kim, S., Sim, Y. & Chang, I. (2003). 'Anti-acne effects of Oriental herb extracts: a novel screening method to select anti-acne agents', *Skin Pharmacol Appl Skin Physiol.*, 16(2), pp. 84-90.
84. Kellet, S. & Gawkrödger, D. (1999). 'The psychological and emotional impact of acne and the effect of treatment with isotretinoin', *Br J Dermatol.*, 140(2), pp. 273-282.
85. Tan, J. (2004). 'Psychosocial impact of acne vulgaris: evaluating the evidence', *Skin Therapy Lett.*, 9(7), pp. 1-3.
86. Kucharska, A., Szmurko, A. & Sinska, B. (2016). 'Significance of diet in treated and untreated acne vulgaris', *Postepy Dermatol Alergol.*, 33(2), pp. 81-86.
87. Emiroglu, N., Cengiz, F. & Kemeriz, F. (2015). 'Insulin resistance in severe acne vulgaris', *Postepy Dermatol Alergol.*, 32(4), pp. 281-285.
88. Smith, R., Mann, N., Braue, A., Makelainen, H. & Varigos, G. (2007). 'A low-glycemic-load diet improves symptoms in acne vulgaris patients: a randomized controlled trial', *Am J Clin Nutr.*, 86(1), pp. 107-115.
89. Arora, M., Yadav, A., Saini, V. (2011). 'Role of hormones in acne vulgaris', *Clin Biochem.*, 44(13), pp. 1035-1040.
90. Ismail, N., Manaf, Z. & Azizan, N. (2012). 'High glycemic load diet, milk, and ice cream consumption are related to acne vulgaris in Malaysian young adults: a case-control study', *BMC Dermatol.*, 12, pp. 13.
91. Adebamowo, C., Spiegelman, D., Danby, F., Frazier, A., Willet, W. & Holmes, M. (2005). 'High school dairy intake and teenage acne', *J Am Acad Dermatol.*, 52(2), pp. 207-214.
92. Adebamowo, C., Spiegelman, D., Berkey, C., Danby, F., Rockett, H., Colditz, G., Willet, W. & Holmes, M. (2008). 'Milk consumption and acne in teenaged boys', *J Am Acad Dermatol.*, 58(5), pp. 787-793.
93. Zhang, H., Liao, W., Chao, W., Chen, Q., Zeng, H., Wu, C., Wu, S. & Ho, H. (2001). 'Risk factors for sebaceous gland diseases and their relationship to gastrointestinal dysfunction', *J Dermatol.*, 35(9), pp. 555-561.
94. Bowe, W., Patel, N. & Logan, A. (2013). 'Acne vulgaris, probiotics, and the gut-brain-skin axis: from anecdote to translational medicine', *Beneficial Microbes*, 5(2), pp. 185-199.
95. Bowe, W. & Logan, A. (2011). 'Acne vulgaris, probiotics and the gut-brain-skin axis - back to the future?', *Gut Pathog.*, 3, pp. 1.
96. Parodi, A., Paolino, S., Greco, A., Drago, F., Mansi, C., Rebora, A., Parodi, A. & Savarino, V. (2008). 'Small intestinal bacterial overgrowth in rosacea: clinical effectiveness of its eradication', *Clin Gastroenterol Hepatol.*, 6(7), pp. 759-764.
97. Barrett, J., Canale, K., Geary, R., Irving, P. & Gibson, P. (2008). 'Probiotic effects of intestinal fermentation patterns in patients with irritable bowel syndrome', *World J Gastroenterol.*, 14(32), pp. 5020-5024.
98. Chiu, A., Chon, S. & Kimball, A. (2003). 'The response of skin disease to stress: changes in the severity of acne vulgaris as affected by examination stress', *Arch Dermatol.*, 139(7), pp. 897-900.
99. Chen, Y. & Lyga, J. (2014). 'Brain-skin connection: stress, inflammation, and skin aging', *Inflamm Allergy Drug Targets.*, 13(3), pp. 177-190.
100. Zouboulis, C., Seltmann, H., Hiroi, N., Chen, W., Young, M., Oeff, M., Scherbaum, W., Orfanos, C., McCann, S. & Bornstein, S. (2002). 'Corticotropin-releasing hormone: an autocrine hormone that promotes lipogenesis in human sebocytes', *Proc Natl Acad Sci USA.*, 14(99), pp. 7148-7453.
101. Zbytek, B., Mysliwski, A., Slominski, A., Wortsman, J., Wei, E. & Mysliwska, J. (2002). 'Corticotropin-releasing hormone affects cytokine production in human HaCaT keratinocytes', *Life Sci.*, 70(9), pp. 1031-1021.
102. Yosipovitch, G., Tang, M., Dawn, A., Chen, M., Goh, C., Chan, Y. & Seng, L. (2007). 'Study of psychological stress, sebum production, and acne vulgaris in adolescents', *Acta Derm Venereol.*, 87(2), pp. 135-139.
103. Seidman, M., Siegel, B., Shah, P. et al. (2013). 'Hemispheric dominance and cell phone use', *JAMA Otolaryngol Head Neck Surg.*, 139(5), pp. 466-470.
104. Koljal, S., Mandar, R., Sober, T., Roop, T. & Mandar. (2017). 'High-level bacterial contamination of secondary school students' mobile phones', *Germs*, 7(2), pp. 73-77.
105. Josse, G., Mias, C., Le Digabel, J. et al. (2019). 'High bacterial colonization and lipase activity in microcomedones', *Exp Dermatol.*, 29(2), pp. 168-176.
106. Saurat, J. (2015). 'Strategic targets in acne: the comedone switch in question', *Dermatology*, 231, pp. 105-111.
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