



www.CosmeticFormulators.com

Bill@CosmeticFormulators.com

500-DALTON RULE

Human skin has unique properties of which functioning as a physicochemical barrier is one of the most apparent. The human integument (tough outer protective layer) can resist the penetration of many molecules. However, especially smaller molecules can surpass transcutaneous. They can go by the corneal layer, which is thought to form the main deterrent. The molecular weight (MW) of a compound must be under 500 Dalton to allow skin absorption. Larger molecules cannot pass the corneal layer.

Arguments for this "500 Dalton rule" are.

- 1) virtually all common contact allergens are under 500 Dalton, larger molecules are not known as contact sensitizers. They cannot penetrate and thus cannot act as allergens in man.
- 2) the most used cosmeceutical agents applied in topical dermatotherapy are all under 500 Dalton.
- 3) all known topical drugs used in transdermal drug-delivery systems are under 500 Dalton. For cosmeceutical development purposes, it seems logical to restrict the development of new innovative compounds to a molecular weight of under 500 Dalton, when topical dermatological therapy or percutaneous systemic therapy.

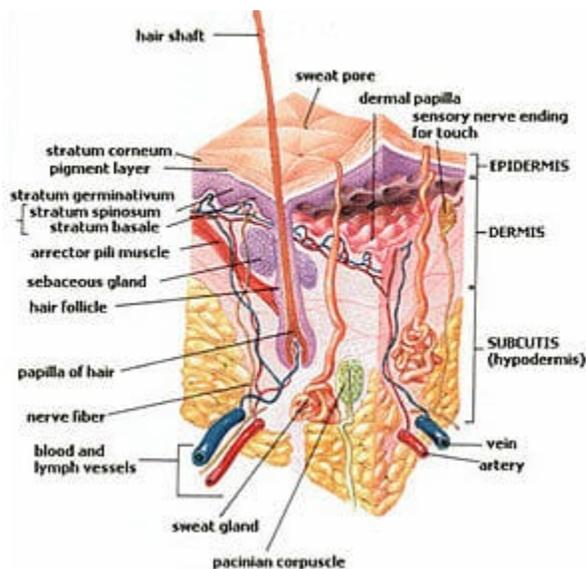
Human skin has unique properties of which functioning as a physicochemical barrier is one of the most apparent. The human integument is able to resist the penetration of many molecules. However, especially smaller molecules can surpass transcutaneously. They are able to go by the corneal layer, which is thought to form the main deterrent. We argue that the molecular weight (MW) of a compound must be under 500 Dalton to allow skin absorption. Larger molecules cannot pass the corneal layer. Arguments for this "500 Dalton rule" are 1) virtually all common contact allergens are under 500 Dalton, larger molecules are not known as contact sensitizers. They cannot penetrate and thus cannot act as allergens in man; 2) the most commonly used pharmacological agents applied in topical dermatotherapy are all under 500 Dalton; 3) all known topical drugs used in transdermal drug-delivery systems are under 500 Dalton. In addition, clinical

experience with topical agents such as cyclosporine, tacrolimus and ascomycins gives further arguments for the reality of the 500 Dalton rule. For pharmaceutical development purposes, it seems logical to restrict the development of new innovative compounds to a MW of under 500 Dalton, when topical dermatological therapy or percutaneous systemic therapy or vaccination is the objective.

The 500 Dalton Rule states that molecules greater than 500 Daltons cannot penetrate the skin barrier. So what exactly does that mean?

We've mentioned the 500 Dalton Rule several times in articles as a general rule of thumb for ingredients that need to penetrate the skin. This rule of thumb is generally the standard for pharmaceuticals and medicine and is often relied on for cosmetic practices. Though this rule has been proven generally effective right now, in the future, studies will look at what other factors — such as delivery methods — could mean for the size molecules must be for skin penetration.

How Does Skin Work?



The skin is a very complex organ and while size is crucial for penetration and absorption, other factors can affect this.

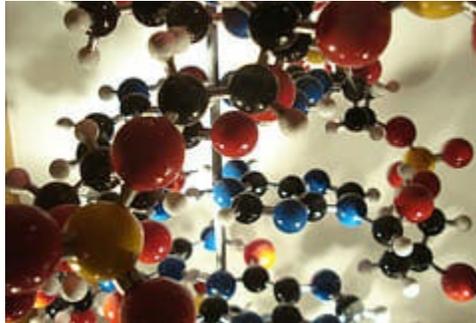
It's easy to take the skin for granted — after all, we look at it every day and we sometimes forget how incredibly complex it is. The skin is, after all, the largest organ the body has, making up about 16% of body weight ([University of Washington](#)).

The outer layer is the epidermis, which is comprised of keratinocytes, or skin cells. Out the outermost part of this is the stratum corneum — which is comprised of dead keratinocytes that shed constantly. Underneath that are the living layers of keratinocytes, called the squamous cells. At the innermost layer of the epidermis are the basal cells, which divide continuously to form new keratinocytes.

In between the epidermis and lower dermis are the melanocytes, which are responsible for forming your skin color. The dermis is where the blood and lymph vessels that become more numerous the deeper you go are located ([Encyclopedia of Women's Health](#)). Underneath this is the subcutis, which houses loose connective tissue and fat ([Skin Structure and Function](#)).

Of course, there is more to skin than this explanation, but this gives you some idea. These layers together make up the skin and serve as a barrier to block substances from getting into the body.

So How Do Ingredients Penetrate Skin?



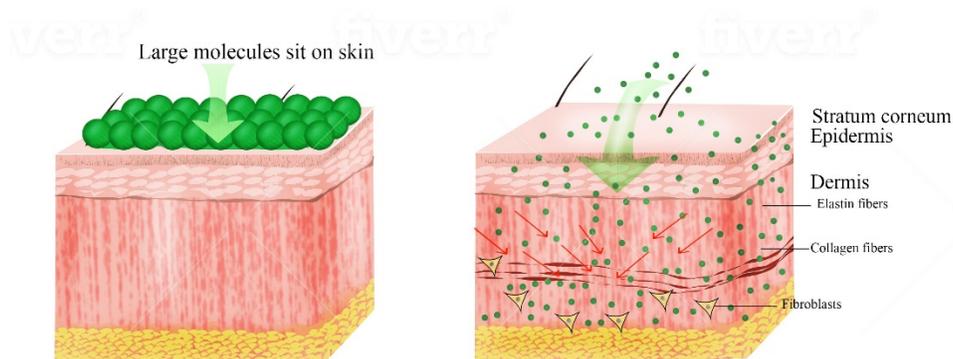
Though the skin acts as a barrier, certain molecules can penetrate it.

While skin may be a barrier, it's not totally impenetrable.

Molecules that are of a small enough weight are able to penetrate through the layers of the skin and be absorbed. This weight is generally considered to be 500 Daltons ([Experimental Dermatology](#)). After review, researchers found that there were no ingredients that were effective when much larger than 500 Daltons, though there are some that are still effective at slightly larger than 500 Daltons. Common allergens also tend to be under 500 Daltons.

And, yet there are still some exceptions to this rule. For example, atopic dermatitis can be treated with derivatives tacrolimus, which is 822 Daltons, and ascomycin, which is 811 Daltons. But, generally speaking, researchers suggest that anything intended for medicinal purposes be smaller than 500 Daltons to assure absorption.

ALOE VERA 10X-D



Most aloe

Most aloe is over 2000 daltons, too large to be absorbed by our skin

Aloe vera 10x-D

Aloe vera 10X-D 50-400 daltons, the perfect size molecules or skincare molecules

What Does that Mean for Skin Care?

While the 500 Dalton Rule could have exceptions, right now, many formulators rely on it.

That doesn't necessarily mean that skin care is ineffective above 500 Daltons, but for products that need to get to the lower layers of skin, it should be below 500 Daltons. Some products, for examples occlusive moisturizers, which sit on top of the skin and prevent transepidermal water loss (TEWL), don't need to be absorbed into the skin. However

There is some information that suggests that delivery system plays a role ([Spa Finder](#)). But the researchers who declared the 500 Dalton rule were not able to find any proven topical medications that existed above 500 Daltons ([Experimental Dermatology](#)). Some medicines employ the use of super small nanoparticles to act as carriers because of their size. However, further research on their effectiveness and risk assessment needs to be done ([Dermato Endocrinology](#)).

Bottom Line

When ingredients are intended to penetrate the skin for treatment of one kind or another, they should generally fit within the 500 Dalton rule. While there's a complex system to the pathways an ingredient can take to be absorbed, there are many reasons why the 500 Dalton rule is considered the standard. There are no topical medications that have been effective much above 500 Daltons, nearly all known allergies are less than 500 Daltons, and the most commonly used pharmaceuticals agents are below 500 Daltons. However, the issue of skin penetration is complicated and further studies will uncover if it is possible that delivery systems and methods of entry could allow larger molecules to pass through skin.