

## Abstract

Nutrition is a complex subject as the effects of correct nutrition are indirect and slow to appear. This is particularly true for hair which is slow to respond to any form of treatment. Correct nutrition has been shown by many trials to be essential for healthy hair growth, and conversely many deficiencies correlate with hair loss. Hair nutrition is therefore a vital part of any treatment regime. A truly systematic and rigorous approach must be taken when formulating a nutritional supplement for hair due to the many factors that affect the eventual efficacy of the treatment. Several of these factors are discussed with applicable examples to demonstrate the importance of careful formulation.

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## Introduction

The fact that hair growth requires complex nutrients and a ready supply of oxygen is well documented, but often overlooked. Perhaps because the effects are indirect and difficult to measure, comparatively few studies have trialled ingredients and combinations of ingredients to maintain or promote hair growth. It is not surprising then that many respectable manufacturers of nutritional supplements do not consider the importance of bioavailability, balancing elements with shared uptake pathways, and fail to ensure that no component has a negative effect on the absorption or action of other components in the formula.

Just as surely as hair will not begin to grow without appropriate growth factors and external stimuli, hair will not continue to grow without adequate circulation and nutrition. A balanced, bioavailable formula to protect and maintain hair growth is vital.

## Concentration

There is a habit among supplement formulators to include the maximum possible level of everything, “bigger is better” and they want their label to look better than the next one.

It is well known that this is not necessarily correct. The most obvious and common example in hair loss supplements is saw palmetto. Opinions vary about the efficacy of saw palmetto *in vivo*, but there is strong evidence from tissue sample experiments that saw palmetto inhibits the 5 $\alpha$  reductase enzyme responsible for converting testosterone to dihydrotestosterone<sup>[1]</sup>. Component analysis shows that certain fatty acids but particularly lauric acid and oleic acid are responsible for the activity of saw palmetto<sup>[2]</sup>. Saw palmetto extract is a refined version of the whole fruit form, and retains a high percentage of the fatty acid content whilst removing other less useful components.

Therefore it is apparent that a significantly lower dose of the extract is required to deliver the same levels of active fatty acids, one calculation estimates that 320mg of extract would have the fatty acid component of 1500mg of the whole fruit form. An

additional consideration is the selective inhibition of the two isoforms of 5 $\alpha$  reductase. It has been shown in limited *in vitro* tests that both isoforms may be inhibited by lipid-rich saw palmetto extracts<sup>[3]</sup>, however there has been no study finding a measurable effect on both isoforms from the whole fruit form. Of course the whole fruit contains all of the components of the extract and so theoretically would have the same effect, however this has not been proven.

## Bioavailability

Many common vitamins and all amino acids exist as multiple isomers, however it is rare that both or even all forms are equally available to human metabolism. The chirality of amino acids is well established, as is the dramatic difference between left and right enantiomers in the human body. On the whole, humans can only metabolise left or L enantiomers, such as L-Cysteine. R-Cysteine is not taken up or commonly metabolised, therefore commonly used racemic mixtures of the two forms are only half comprised of useful amino acids.

Vitamins, such as vitamin B<sub>6</sub> also have several forms, pyridoxine is the form of vitamin B<sub>6</sub> most commonly used in nutritional supplements, however it is not the bio-active form. Instead it must be phosphorylated to become pyridoxal 5 phosphate, which is active as an enzyme cofactor for many reactions, and is important for uptake of other nutrients as well<sup>[4]</sup>. The phosphorylation reaction to activate pyridoxine takes energy and a certain set of conditions, and therefore not all the pyridoxine taken in a supplement is used. A more efficient alternative is to use pyridoxal 5 phosphate in the supplement, so the bio-active form is immediately available, requiring no energy, and minimal wastage.

Bioavailability is not just controlled by isomeric forms. Nutrient uptake is complex, and there are many surprising instances where one nutrient is dramatically affected – either negatively or positively, by a completely different nutrient in the formula. Pyridoxal 5 phosphate increases L-cysteine incorporation into keratin<sup>[5]</sup>, however as pyridoxal 5 phosphate may be a cofactor of

the enzyme responsible for incorporating L-cysteine into hair, this is unsurprising. More interesting are the studies showing that both green tea and saw palmetto inhibit the absorption of iron. Whilst the mechanism for this is not entirely described, it is thought to be due to the concentrations of tannic acids in both<sup>[6]</sup>. Tannic acid levels are not significantly reduced when they are used in their purified extract form.

Therefore a formula must be designed so not only are bioavailable forms used, but the whole formula is studied for negative interactions and targeted towards a particular concern.

## Balance

Unfortunately a formula containing all of the nutrients necessary without a single negative interaction is rarely possible. Therefore balance is essential, especially where nutrients compete for uptake via the same pathways.

Balance is not simply a matter of including every competing element at the same percentage. Certain nutrients will compete more successfully than others, and all elements for healthy hair are necessary at different levels. The ion uptake channel for copper, zinc and magnesium ions is a useful illustration as the balance between the three competing elements is fine, and taking too much of one will decrease the other two. It has been shown separately that copper, zinc, and magnesium are important for hair growth. As well as their role in nutrition and enzyme action, Copper and zinc have also both been shown to inhibit 5 $\alpha$  reductase, although zinc has only been proven to inhibit the type 1 isoform found in skin not hair<sup>[7,8]</sup>. Magnesium has been shown to correlate with certain diffuse alopecias in women<sup>[9]</sup>, but the precise cause has not been established.

However it would not be correct to create a supplement with more copper, slightly less zinc, and lower magnesium content due to their proven importance. In fact as magnesium is required at higher levels around the body comparatively it should be included at a higher dose, followed by zinc, and then copper is useful even at low percentages.

## Component Synergy

It is also vital to consider the opposite possibility in complex formulae. Combinations of nutrients may improve the results of the two nutrients separately, such as the combination of curcumin and resveratrol. Resveratrol has been extensively studied both as an anti-inflammatory and anti-angiogenic agent, however results have been limited. Curcumin has also not lived up to initial promise as an anti-inflammatory. However it has been shown that the two work synergistically in a cancer model<sup>[10]</sup>, to decrease inflammation and possibly angiogenesis, although even in combination a significant anti-angiogenic effect *in vivo* seems unlikely<sup>[11]</sup>.

Correct synergy can even result in a measureable effect where neither ingredient was effective separately. L-cysteine and pantothenic acid can be useful as they are incorporated into

keratin; pantothenic acid in particular is very common in the form of panthenol, the conditioning agent. However a combination of the two has been suggested by *in vitro* tests to help increase hair repair and keratinocyte proliferation<sup>[12,13]</sup>.

There are also several obvious examples where two ingredients act together, and these should not be ignored. For instance it is well known that vitamin B<sub>12</sub> and iron are both necessary for erythrocyte formation, and hence oxygen circulation, so it is important that a supplement contain both to significantly help this process.

## Circulation

A final, and often overlooked, factor to consider is the circulation of oxygen and nutrients to the hair. Even a perfectly balanced supplement would not be effective if there was no blood flow to the hair. Many believe that several forms of hair loss are caused or exacerbated by a deficient blood supply to the hair follicle, and so it is possible that nutrients from a supplement could not reach the follicle in useful quantities. Therefore it may be beneficial to increase the circulation. This can be achieved through topical treatments that stimulate nitric oxide production or angiogenesis. However a simpler solution may be to include a known stimulant like taurine or caffeine to increase bloodflow around the entire body.

The stimulatory effects of caffeine and taurine on nutrient uptake and metabolism may also be beneficial. An added consideration is the possible effect of caffeine upon dihydrotestosterone and hair loss. Caffeine has been shown by several studies to reduce hair loss caused by dihydrotestosterone, the *in vivo* studies were successful topically<sup>[14]</sup>, but the effects of oral caffeine have not been tested at this time. Taurine has also been shown by *in vitro* testing to protect the hair from TGF $\beta$ -1 induced apoptosis<sup>[15]</sup>.

## Conclusion

In spite of the paucity of clinical data in the area, it is possible through careful formulation to develop a potent, bioavailable, and balanced formula with combinations of ingredients that are likely to have good clinical outcomes. This is particularly true if supplements are used to support wider treatment regimes - even surgery.

Intervention utilises all of the above knowledge and technology. Nanogen have developed two targeted Intervention formulae, for Men and for Women, to give the best results possible. It is not possible, or even desirable, to include every possible anti-hair loss ingredient in one tablet, as shown by issues such as bioavailability and shared uptake pathways. For example, Intervention for Men does not contain iron or vitamin B<sub>12</sub> as anaemia is rarely a cause of hair loss in men. Intervention for Women does not contain saw palmetto or green tea. As iron is especially important for women, it is vital that iron uptake is not blocked by these ingredients.

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