

CHAPTER 15

CRINAGEN™

Long is the road from conception to completion.

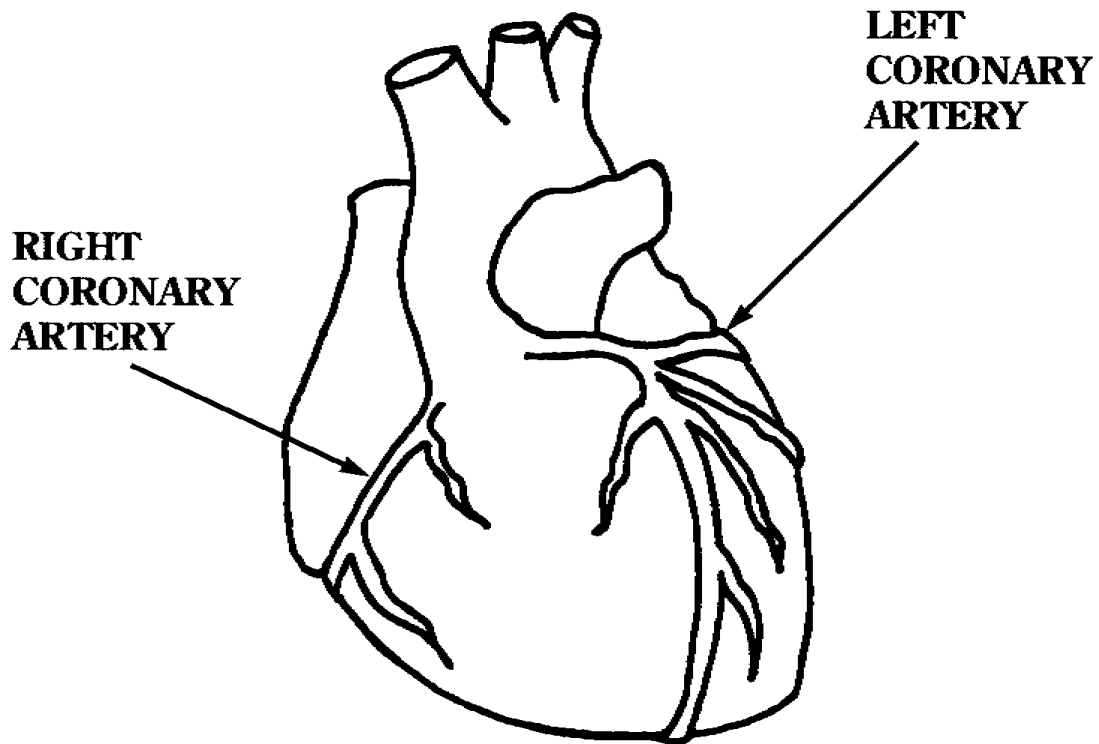
Molière

Crinagen™ (trademark name, Raztec Enterprises) is a completely natural topical scalp preparation marketed by Raztec Enterprises. Its natural ingredients perform three basic functions.

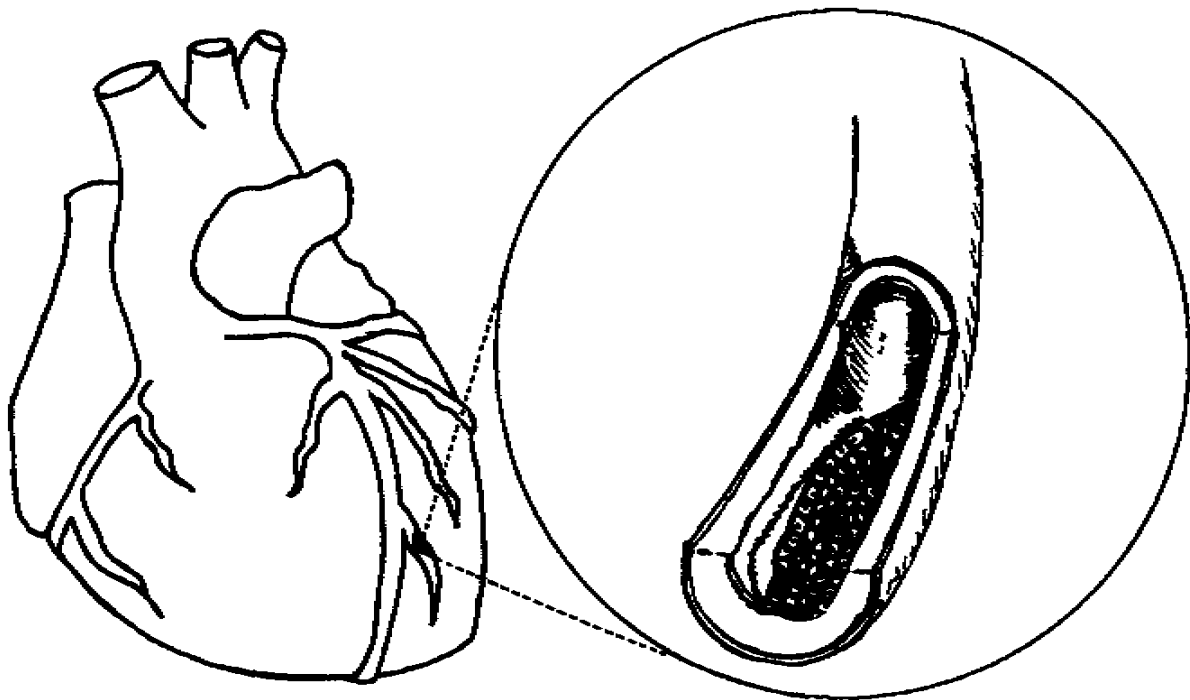
1. Crinagen™ blocks the activity of the enzyme [5 alpha-reductase](#) and thus reduces the production of [dihydrotestosterone](#) within the scalp. Dihydrotestosterone is a more active and potent form of testosterone usually produced at its site of action. The enzyme 5 alpha-reductase is necessary for its production. Most researchers believe that this hormone is responsible for the progressive miniaturization of hair follicles, which is the hallmark of [androgenic alopecia](#). By lowering the concentration of dihydrotestosterone in the scalp, Crinagen™ is an effective [antiandrogen](#).

2. Crinagen™ affects blood vessels that nourish hair follicles within the scalp. The ingredients within Crinagen™ both vasodilate the blood vessels supplying the scalp as well as affect the characteristics of blood delivered to the scalp. Hair follicle size is directly related to the blood vessels that supply it: that is, the larger the blood vessels that supply it, the larger the hair follicle. Augmenting blood supply to the hair follicle increases its size and therefore increases the production of hair. Thus, by increasing the blood supply to hair follicles, Crinagen™ is an effective hemodynamic enhancer.

3. Crinagen™ reduces inflammation which is associated with hair loss. The natural ingredients found within Crinagen™ have been demonstrated to decrease the inflammatory reaction as well as have antibacterial effects. Bacteria found within the scalp have been



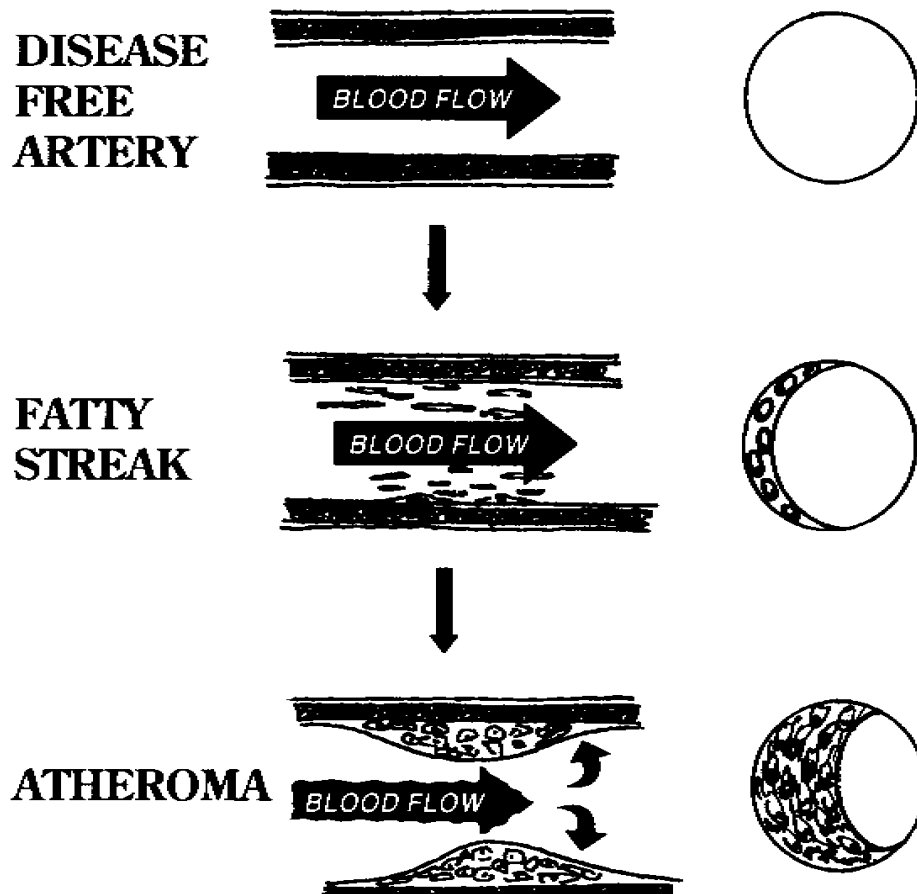
demonstrated to produce an inflammatory reaction. Its antibacterial effects and ability to decrease the inflammatory response make Crinagen™ an effective anti-inflammatory agent.



These three properties will now be discussed in greater detail, but, prior to this discussion, let's address an important issue. Unlike most other topical scalp preparations, Crinagen™ does not claim to promote hair regrowth. This is because, as decided by the [FDA](#), it is unlawful to make claims that are not substantiated. Despite this warning, there are still many manufacturers that continue to falsely claim that their products can grow hair. Unfortunately, criminal prosecution is both time consuming and expensive, and the FDA has practically abandoned this practice.

In

1988,



Minoxidil (Rogaine®, registered trademark name, The Upjohn Company) was the first drug ever approved by the FDA for the treatment of androgenic alopecia. Since then, no other drug has been approved by the FDA for this purpose. Thus, any product claiming to promote the growth of hair, with the exception of Minoxidil, is making unlawful and, more importantly, unsubstantiated claims. This is not to say that other agents or therapies are ineffective in promoting the

regrowth of hair, but, rather, that they have not been recognized by the FDA to do so. Until they are, it is unlawful for manufacturers to advertise that these products are able to promote the regrowth of hair.

Another problem with many of the topical preparations being sold is that they are vague about what they contain and how their ingredients work. The ability of manufacturers to sell these different lotions and concoctions rests in the hope that they might promote hair growth. Other manufacturers don't want to reveal their "secret" ingredients, but continue to claim that these formulas, nonetheless, promote the growth of hair.

One of the most unique aspects of Crinagen™ (trademark name, Raztec Enterprises) is that it does not have just one active ingredient, but many. These ingredients act together to help block factors that are detrimental to hair growth. In fact, Crinagen™ can also be used with other agents to block these detrimental factors. The following discussion describes the antiandrogenic, hemodynamic and anti-inflammatory effects of Crinagen™.

ANTIANDROGENIC EFFECTS

The two most powerful ingredients within Crinagen™ are zinc and [saw palmetto](#). A more detailed explanation of both these antiandrogens is provided in Chapter 7 ("Zinc") and Chapter I I ("Nutrition and Hair"). Both agents have been shown to be powerful antiandrogens, which block the conversion of testosterone into dihydrotestosterone [1,2,3,4,5]. Recall that the enzyme responsible for the production of dihydrotestosterone is called 5 alpha-reductase (Figure 15-1). In addition, Crinagen™ contains vitamin B6, which has been shown to work in concert with zinc to inhibit 5 alpha-reductase [1].

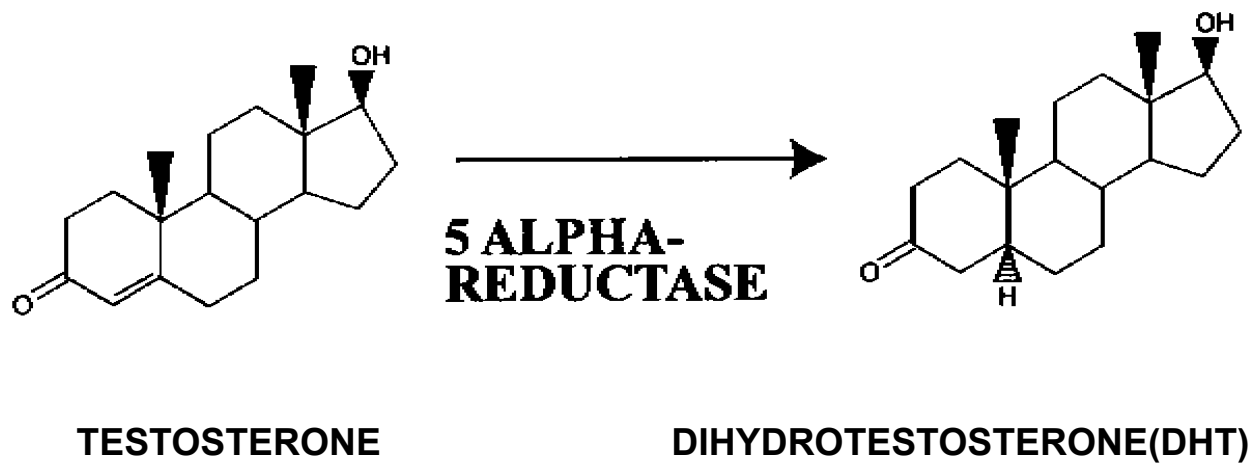


FIGURE 15-1 (above) Conversion of testosterone into dihydrotestosterone by 5 alpha-reductase.

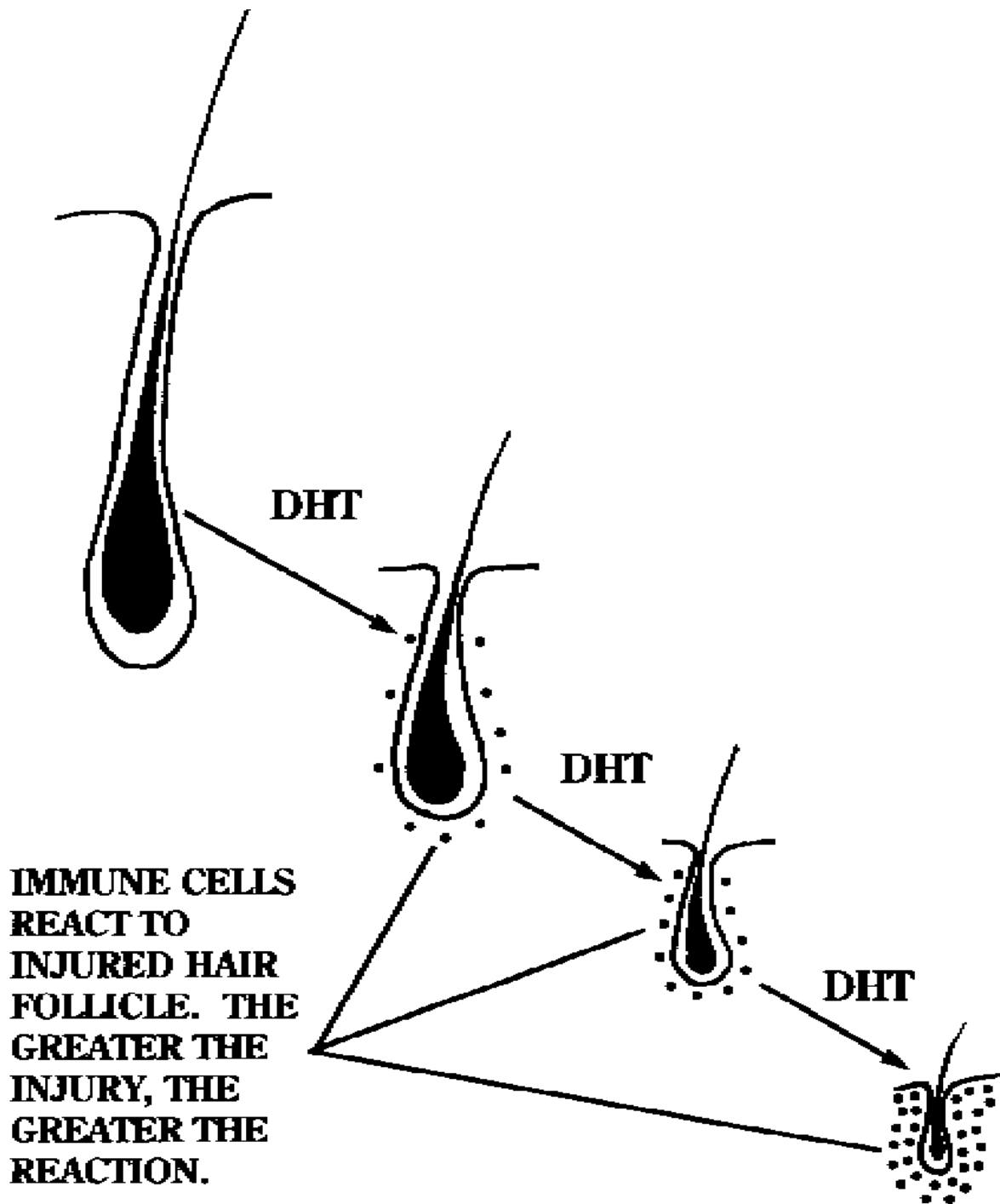


FIGURE 15-2 (above) While dihydrotestosterone (DHT) continues to miniaturize the hair follicle, it also damages it. The immune system

responds to this damaged hair follicle by producing an inflammatory response which eventually destroys the follicle.

The hallmark of androgenic alopecia is the progressive miniaturization of hair follicles. This is caused by a genetic predisposition of individual hair follicles which renders them more sensitive to normal circulating levels of androgens (male sex hormones). Increased levels of 5 alpha-reductase in these genetically predisposed hair follicles causes the conversion of male sex hormones (androgens) into dihydrotestosterone, the hormonal culprit responsible for androgenic alopecia. Dihydrotestosterone continues to damage and miniaturize hair follicles (Figure 15-2).

As hair follicles are damaged by the ongoing effects of dihydrotestosterone, the body responds to this injury with an inflammatory response, primarily mediated by the immune system. The cells of the immune system cause inflammatory reactions which further damage these hair follicles, and most likely lead to their eventual deaths (Figure 15-2). The anti-inflammatory effects of Crinagen™ will be discussed shortly.

In addition to vitamins and minerals, herbs can also affect hair growth. Zinc, which is a mineral, has already been discussed above as well as in its own separate chapter, (Chapter 7, "Zinc"). The current belief is that it acts as an antiandrogen [1,2]. Another naturally occurring substance, saw palmetto, is also believed to work as an antiandrogen. It has been used as an herbal remedy for the treatment of prostatic disease. It is currently marketed in Germany as an over-the-counter medication for the treatment of [benign prostatic hypertrophy](#). Again, prostatic disease is being discussed here because of its similarity to androgenic alopecia, since both conditions depend on the production of dihydrotestosterone. A more detailed discussion concerning the similarities between prostatic disease and hair loss appears in Chapter 6 (The Antiandrogens").

Although formal studies on the use of saw palmetto as an antiandrogen have not been conducted in this country, many have been done in Germany. In one study, an extract of this herb was given to 2080 patients with benign prostatic hypertrophy [3]. Most patients reported an improvement in their symptoms.

Symptomatic complaints of prostatic disease, such as urinary obstruction, are directly related to the size of the prostate. This improvement in symptoms was due to reduction in prostate size. The physicians rated this extract's effectiveness as "good" to "very good" in the treatment of prostatic disease. Of the 2080 patients treated, fifteen of them (0.72 %) had mild side effects.

In yet another study, 1,334 patients with benign prostatic hypertrophy were given an extract of saw palmetto and virtually all of their symptoms (consisting of increased frequency of urination, increased frequency of urination at night, pain during urination, inability to void all the urine from the bladder) were substantially reduced [4]. This herb was rated as "good to excellent" in over 80% of the patients studied. This study concluded that the improvement in the quality of life in these patients with benign prostatic hypertrophy justifies this form of therapy.

Another similar study was performed with forty-two men with benign prostatic hypertrophy [5]. Again, saw palmetto was conclusively proven to be effective in the treatment of benign prostatic disease. The study also demonstrated that the symptoms of benign prostatic disease improved significantly by the sixth month of therapy, at the latest. Also, no side effects were observed.

All of these studies indicate that saw palmetto is an effective antiandrogen. Don't think for one second that because it's only an herb, it's not a true medication. Many of the most effective medications used today are herbs. These include the foxglove plant, Madagascar periwinkle, and the Pacific yew. The foxglove plant is used to make Digoxin, one of the most frequently used medications for treating cardiac disease. The other two, Madagascar periwinkle and the Pacific yew, are used to produce effective anti-cancer medications. Again, just because something is called an herb and is not regulated by the FDA, it doesn't mean that it is not capable of having powerful medicinal effects.

Since saw palmetto is an effective antiandrogen for the treatment of prostatic disease, it may also have applications in the treatment of hair loss. Remember, androgenic alopecia and prostatic disease are related since 5 alpha-reductase is required to convert the hormone

testosterone into dihydrotestosterone for either disease process to occur. If saw palmetto blocks the effects of this enzymatic reaction in prostatic disease, there is a good chance that it might do the same in androgenic alopecia. By blocking the enzyme 5 alpha-reductase and the formation of dihydrotestosterone, this herb has the potential to prevent the progressive miniaturization of hair follicles. In other words, by acting as an antiandrogen, it can block the progressive loss of hair.

In many ways, the proposed mechanism of action of this herb is similar to that of the drug finasteride. Finasteride is a 5 alpha-reductase inhibitor used in the treatment of prostatic disease and will soon be available for the treatment of androgenic alopecia. Whereas side effects of finasteride use include decreased sex drive and impotence, saw palmetto is recommended by herbalists as an aphrodisiac. Again, side effects associated with this herb are essentially nonexistent [3,4,5]. A more detailed discussion concerning finasteride and its utility in treating hair loss is provided in Chapter 6 ("The Antiandrogens").

To use this herb, try taking one gram once a day orally before you consider increasing its dose. Also, as discussed in Chapter 6 ("The Antiandrogens"), if we were to use this herb topically, we could increase its concentration and probably its effect specifically where we want it to act, namely the scalp. This is precisely what Crinagen™ accomplishes, but, rather than being limited to just one active ingredient, it has many. Interestingly, anecdotal reports have emerged from Germany stating that pumpkin seeds may also be beneficial in treating prostate disease. What's really interesting is that pumpkin seeds are loaded with zinc. Is this a coincidence? Of course not: these reports only confirm the antiandrogenic properties of zinc. For information on the incredible antiandrogenic effects of this mineral, I refer you to Chapter 7 ("Zinc").

The best way to stop the progression of androgenic alopecia is to correct the underlying genetic defect that causes it. Unfortunately, gene therapy is not yet possible. The next best solution is to block the formation of dihydrotestosterone. One of the actions of Crinagen™ is to block the activity of 5 alpha-reductase and, thereby, its ability to convert testosterone into dihydrotestosterone [1,2,3,4,5]. In addition,

it contains vitamin B6, which has been shown to work in concert with zinc to inhibit 5 alpha-reductase [1]. In this manner, it reduces the amount of dihydrotestosterone within the scalp. Reducing the amount of dihydrotestosterone not only prevents the progressive miniaturization of the hair follicle, but equally as important, it reduces injury to the hair follicle. Injury to the hair follicle results in an inflammatory response which will further damage it. A more detailed explanation describing the relationship between inflammation and hair loss appears in Chapter 5 ("Inflammation and Hair Loss").

HEMODYNAMIC EFFECTS

Nutritive blood flow to the hair follicles is another factor that has been shown to regulate hair growth. Crinagen™ contains polysorbate 20 and niacin, both of which cause the release of histamine. Histamine mediates the immediate (vascular) response of inflammation, thought to be beneficial for hair growth. In addition, Crinagen™ contains Ginkgo biloba, which has been shown to affect the amount of blood delivered to the hair follicle. [Ginkgo biloba](#) is one of the world's oldest (still existing) plants. Ancient China was the first country to utilize extracts from its leaves for medicinal purposes. The West only started to utilize this amazing plant during the 1960s, when it became technically possible to isolate its extract. This extract contains two major classes of substances: the [bioflavonoids](#) and the [terpenes](#) (sometimes called [ginkgolides](#)) [6].

Bioflavonoids are truly incredible substances which have many different properties. They have been proven to increase the absorption of vitamin C, another important vitamin that has been shown to improve blood circulation. Bioflavonoids strengthen capillary walls and have antibiotic-like properties [7]. They may also lower cholesterol levels [8,9]. Finally, bioflavonoids have also been proven to be potent anti-inflammatory agents. These effects will be discussed shortly.

The terpenes (ginkgolides) have many interesting properties. One of their specific actions is to inhibit [platelet activating factor](#), a major mediator in inflammatory reactions which also affects platelet aggregation. Some hair-promoting agents (minoxidil, cyclosporine, and phenytoin) cause immunosuppression and others (Foltene® [10,

11]) affect the blood vessels that nourish the scalp . By blocking platelet activating factor, terpenes may decrease both inflammation and platelet aggregation.

Bioflavonoids also have effects on blood vessels and on other vitamins that affect blood vessels. Hair follicular size is directly related to the blood vessels that supply it: that is, the larger the blood vessels that supply it, the larger the hair follicle; however, these blood vessels, even in extremely healthy hair, are relatively small compared to other blood vessels in the body. Since bioflavonoids have been demonstrated to strengthen capillary walls, they have the potential to strengthen the smaller vessels that nourish hair follicles.

Definitions and References

5 alpha-reductase: an enzyme that converts testosterone into a much more

potent male hormone called dihydrotestosterone. It is essential for the development of androgenic alopecia.

dihydrotestosterone: a more active

and potent form of the testosterone usually produced at its site of action. The enzyme 5 alpha-reductase is necessary for its production. Most researchers believe that this hormone is responsible for the progressive miniaturization of hair follicles, which is the hallmark of androgenic alopecia.

androgenic alopecia: the medical

term for male-pattern hair loss. it appears to be caused by a genetic predisposition of individual hair follicles to normal circulating levels of androgens (male sex hormones). Other terms for androgenic alopecia include male-pattern baldness, female baldness, common baldness, diffuse alopecia, hereditary alopecia, and, of course, baldness.

antiandrogen: substance that

blocks the effects of androgens or masculinizing hormones.

United States Food and Drug Administration (FDA): agency that regulates drugs, medical devices, cosmetics, and food additives within the United States.

saw palmetto: a natural herb that is an effective antiandrogen.

benign prostatic hypertrophy: an enlargement of the prostate gland that is not related to cancer.

Ginkgo biloba: a natural herb derived from one of the world's oldest existing plants.

bioflavonoids: naturally occurring substances that strengthen capillary walls and have many other incredible properties.

terpenes: equivalent to ginkgolides, they were discovered to inhibit platelet activating factor.

ginkgolides: equivalent to terpenes, they were discovered to inhibit platelet activating factor.

platelet activating factor: a major mediator of inflammatory reactions. It also affects platelet aggregation.

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CHAPTER 15 (continued)

CRINAGENTM

Bioflavonoids can also increase the absorption of vitamin C. The interesting fact about vitamin C is that, like vitamin E, it can improve the circulation. Other vitamins that improve circulation include niacin and coenzyme Q10. Although there are anecdotal reports that both of these nutrients promote hair growth, none of them exist in the medical literature. By strengthening vessels and improving the blood circulation to nourish hair follicles, these vitamins provide yet another mechanism for preventing or minimizing hair loss.

One study examined Ginkgo biloba's role in promoting hair growth in an animal model [12]. The researchers who conducted this study concluded that Ginkgo biloba promoted hair regrowth. They attributed this effect to Ginkgo biloba's inhibition of blood platelet aggregation, thrombin activity, and fibrinolysis. What this means is that this herb, like Foltene ® [10,11], appears to affect the amount of blood that is delivered to hair follicles. The researchers also stated that it inhibited a rise in serum triglyceride levels in animals which were fed a high cholesterol diet. Finally, they concluded that these results indicate that Ginkgo biloba can be used as a hair tonic.

Recall that follicular size is directly correlated with blood supply: the larger the blood vessels that supply it, the larger the hair follicle. By affecting the blood supply to the hair follicle, we can hopefully increase its size. In this way, we would reverse the miniaturization of hair follicles by dihydrotestosterone (Figure 15-3).

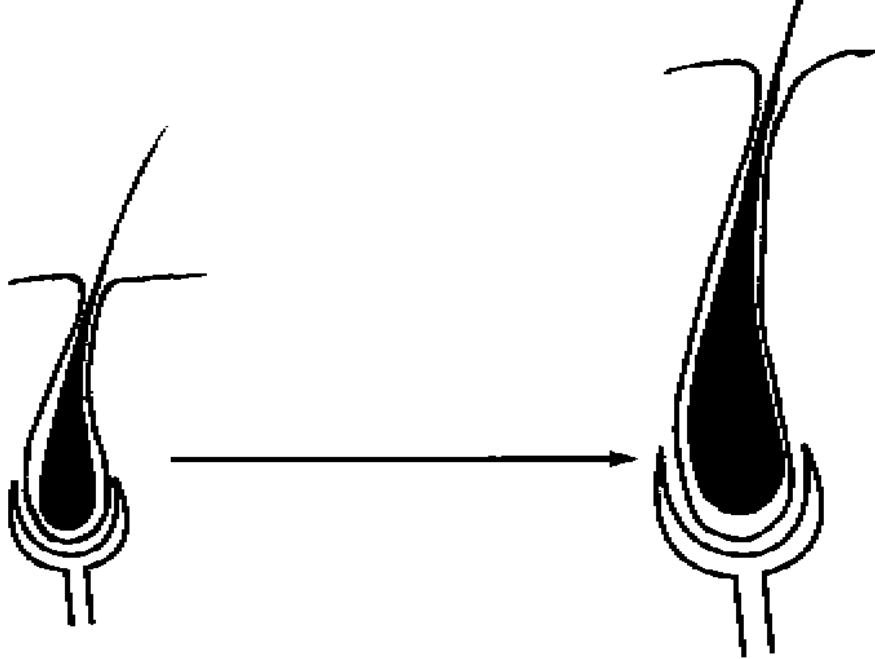


FIGURE 15-3 Crinagen™ (trademark name, Raztec Enterprises) affects blood-flow delivered to the hair follicle and, thereby, may increase the supply of nutritive blood to the hair follicle. Note that follicular size is directly correlated with blood supply: the larger the blood vessels that supply it, the larger the hair follicle.

ANTI-INFLAMMATORY EFFECTS

Crinagen™, again, contains Ginkgo biloba which has many actions that would presumably allow it to contribute to the treatment of hair loss. The bioflavonoids (contained within Ginkgo biloba) are potent anti-inflammatory agents which also have antibiotic-like effects. Inflammation is yet another factor now associated with hair loss [13,14,15]. Bioflavonoids can potentially reduce factors that contribute to hair loss (Chapter 5, "Inflammation and Hair Loss") both by being anti-inflammatory agents and by having antibiotic-like activities.

Propionibacterium acnes is a bacterial species found in the scalp, and many researchers now believe it contributes to inflammation and eventual hair loss. Young et al. [13] have an interesting idea: they propose that these bacteria inhabit certain areas within the hair follicle. These bacteria (Propionibacterium acnes) can cause an inflammatory reaction by three different mechanisms. First, they

activate a portion of the immune system called complement [16]. Second, these bacteria attract certain cells in the immune system (called mononuclear cells), by a process called chemotaxis [17]. Finally, these bacteria produce porphyrins which are pigmented structures [18] that, in the presence of light, can activate complement [19, 20].

These light-activated bacteria have been implicated as the cause of inflammatory reactions that result in other problems. For example, Saint-Leger et al. believe that the porphyrins made by these light-activated bacteria lead to the production of an inflammatory reaction in acne [21]. The clinical observations of Hamilton and Ludwig also indicate that inflammation due to light exposure may be involved in hair loss. Both of them noticed that the early stages of hair loss involve areas of the scalp exposed to sunlight, such as the hairline part or the vertex whorl.

Since it may seem hard to believe that all these problems are caused by bacteria, I will briefly discuss another, unrelated species of bacteria that causes inflammation, ulcers and, possibly, cancer in the stomach. The existence of *Helicobacter pylori*, a bacterial species that is able to live in the acidic environment of the stomach, was determined in 1982. Prior to its discovery, it was generally accepted by the medical community that stomach and intestinal ulcers were caused by the excess secretion of acids in the stomach. It is now widely accepted that *Helicobacter pylori* plays a major role in stomach inflammation and in intestinal and stomach ulcers [22]. In addition, recent evidence suggests that it may also have an important role in the development of stomach cancer [23]. The rate at which ulcers heal is greatly improved if *Helicobacter pylori* infection is suppressed, and, if the infection is eliminated, the recurrence rate (how often an ulcer will reappear) is reduced [24]. The chances of developing a stomach ulcer are at least three to four times higher than normal if the individual has a *Helicobacter pylori* infection [25]. For these reasons, it is now standard treatment to eliminate this bacteria in any infected patient who has either intestinal or stomach ulcers [26].

The purpose of this discussion was to demonstrate that the discovery of one bacterial species can completely change the understanding of a disease process. Whether *Propionibacterium acnes* will indeed affect our understanding of androgenic alopecia remains to be seen. In any case, the possibility that both this bacteria and the inflammatory condition it causes are potential factors in the development of androgenic alopecia warrants further investigation.

I recommend the use of immunosuppressant agents in conjunction with Crinagen™ because, although Crinagen™ may reduce the quantity of dihydrotestosterone within the scalp, it does not completely reverse the damage to hair follicles that has already occurred. These damaged hair follicles incite an inflammatory response by the immune system which can damage them even further. The use of immunosuppressants can reduce this inflammatory reaction and, thus, subsequent damage to hair follicles (Figure 15-4).

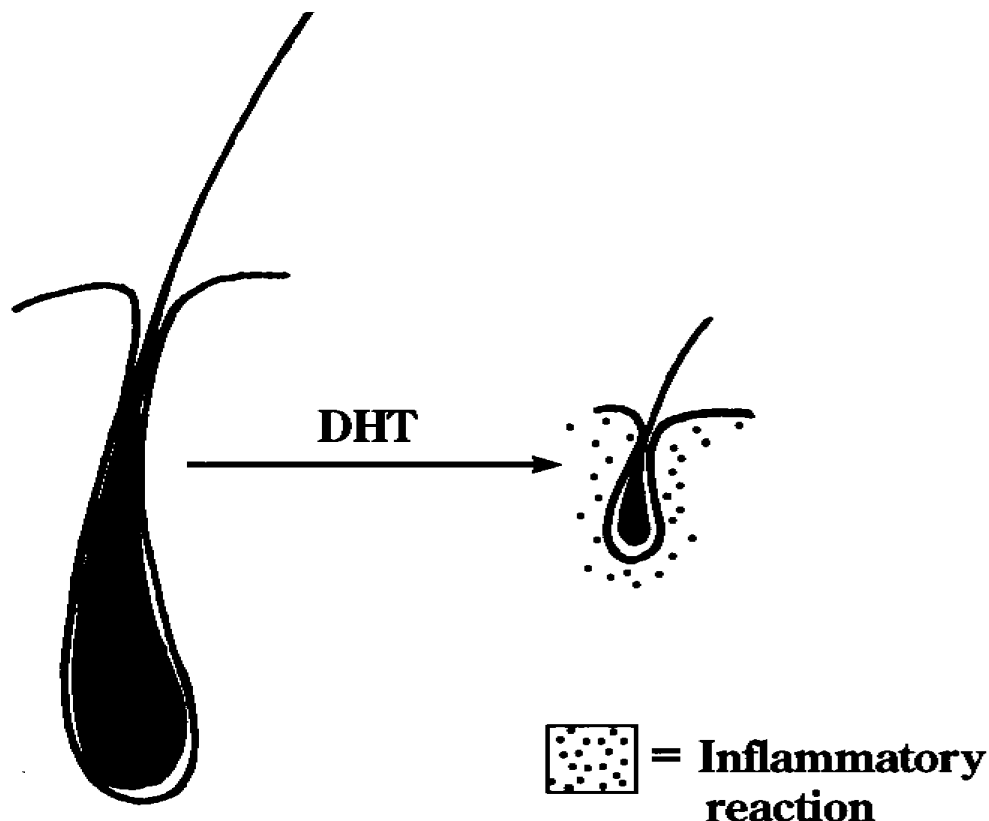


FIGURE 15-4

Dihydrotestosterone (DHT) causes the progressive miniaturization of hair follicles, which is the hallmark of androgenic alopecia. Once damaged, these hair follicles incite an inflammatory reaction which will destroy them. For this reason, the use of immunosuppressant agents in conjunction with Crinagen™ (trademark name, Raztec Enterprises) is highly recommended.

Which immunosuppressant should one use? Recall that the immunosuppressants mentioned in this book include minoxidil, cyclosporine, phenytoin, and the anti-inflammatory shampoos (one of which contains ketoconazole). Aside from shampoos, I would recommend using Minoxidil for two reasons: it is probably the only agent most people have access to and, more importantly, it has been shown to work synergistically with antiandrogens (please refer to Chapter 8, "Minoxidil").

Another unique feature of Crinagen™ in comparison to other topical scalp preparations is that it is sold by itself, without an accompanying shampoo. The reason for this is that effective shampoos already exist. I would recommend ones that are anti-inflammatory, such as Nizoral® (trademark name, Janssen Pharmaceutica) or T-Gel® (trademark name, Neutrogena). Of these two, Nizoral® shampoo is probably a more effective immunosuppressant, but it is a prescription drug. As such, its dose, application frequency, and duration of use must be approved and monitored by a physician.

To prevent the inflammatory reaction to the scalp from occurring, the source of damage to the hair follicles must be abolished. Again, dihydrotestosterone is the source of this injury. It causes the progressive miniaturization of hair follicles. Crinagen™ contains

both zinc and saw palmetto, which reduce the production of dihydrotestosterone by inhibiting the enzyme 5 alpha-reductase (Please refer to Chapters 7, "Zinc", and 11, "Nutrition and Hair"). In addition, it contains vitamin B6, which has been shown to work in concert with zinc to inhibit 5 alpha-reductase (Chapter 7, "Zinc").

Please note that in the above discussions, it is never stated that Crinagen™ promotes hair growth, since this claim still has to be substantiated. Although there is a tremendous amount of research to support that the application of Crinagen™ would be effective in treating hair loss, legitimate clinical research is necessary to substantiate this claim. I openly invite any physician or researcher who can obtain an approved research protocol to contact me. My goal is to determine the effectiveness of Crinagen™, either by itself or combined with other agents, in the prevention of hair loss and in the promotion of new hair growth.

In summary, Crinagen™ is a completely natural combination of substances. They act in three ways: they act as antiandrogens; they affect the nutritive blood supply to hair follicles; and, they act as anti-inflammatory agents. When used by itself or in combination with immunosuppressants, Crinagen™ decreases the production of dihydrotestosterone, which miniaturizes the hair follicle. Furthermore, it inhibits the inflammatory reaction that will ultimately destroy the hair follicle.

Definitions and References are below.

ADDITIONAL INFORMATION

To obtain more information about Crinagen TM (trademark name, Raztec Enterprises) please write to or call:

Raztec, Inc.

P.O. Box 3891

Charlottesville, VA 22903-0891

Phone: (toll-free) 1-888-385-5424

Phone: (from outside the USA or Canada)

1-716-688-4526

Definitions

Propionibacterium acnes: a bacterial species found in hair follicles. For a variety of reasons, researchers believe these bacteria incite an inflammatory reaction which may be a factor contributing to hair loss.

bacteria: the simplest of all known organisms.

complement: a complex of serum proteins that, once activated, destroy bacteria or other invading organisms.

mononuclear cells: cells of the immune system.

chemotaxis: a process whereby mononuclear cells are attracted to some type of agent, i.e. bacteria.

porphyrins: pigmented structures widely distributed in nature.

vertex whorl: the top, back part of the head, where hair has a circular arrangement. Frequently, this is one of the first sites of hair loss.

Helicobacter pylori: a bacterial species that is able to survive in the acidic environment of the stomach. There is evidence suggesting that these bacteria have a major role in the development of stomach inflammation, ulcers, and cancer.

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