

KINETIN- A PROMISING NEW TREATMENT TO PRESERVE HEALTHY, ATTRACTIVE SKIN

New Treatment for Aging Skin

Kinetin is a newly developed ingredient for skin treatment formulated to allow the appearance and texture of skin to be better preserved through advancing years. Recently published scientific evidence based on a well-established in vitro model of cellular aging demonstrates the ability of Kinetin to prevent either completely or partially a variety of aging related changes in the appearance and function of human skin cells.¹ Furthermore, this study found that Kinetin, a synthetic plant growth hormone, does not alter the normal cellular life span or ability of cells to multiply. Consequently, it seems unlikely that Kinetin will exhibit the skin cancer-promoting characteristics of a variety of other agents that have been tested for use in revitalizing aging skin. The combination of effectiveness in maintaining normal cell function and appearance and safety for topical use could make Kinetin the ingredient of choice for preserving healthy, attractive skin.

Kinetin (6-furfurylamino-purine) is a highly potent growth factor that, along with other plant growth substances, promotes cell division and ensures orderly growth and development of plants.² There are a number of plant growth factors known as cytokinins. The most active naturally occurring cytokinin is zeatin, which was originally isolated from corn (*Zea mays*). The synthetic cytokinin that has been most extensively investigated in research studies is Kinetin. Cytokinins resemble the ubiquitous purine compound adenine. The relationship, if any, between the mechanism of action of the cytokinins and their resemblance to adenine is not known, however.

Cytokinins prevent the senescence (aging) of leaves. In many plants, the lower leaves turn yellow and drop off as the upper, new leaves develop. If Kinetin is applied to the lower leaves, they remain green. Similarly, cut leaves remain green when maintained in a nutrient solution containing Kinetin.

More importantly, Kinetin has been shown capable of delaying or preventing a host of age-related changes of human skin fibroblasts grown in laboratory culture.

Fibroblasts are believed to be at the center of age-related changes in the skin. These cells produce collagen and elastin, the two proteins most clearly tied to the development of wrinkles, sagging and laxity of the skin. Fibroblasts have been shown to decrease in number and vitality as the skin ages not only in vitro, but also in vivo. The number of fibroblasts decreases at least 50% between birth and the age of 80 years.³ Older fibroblasts appear shrunken and narrow with diminished cytoplasm.⁴

Table 1. Kinetin's effects on cytological manifestations in *in vitro* aging

Characteristic	Untreated		Kinetin	
	Young	Old	Young	Old
Cell enlargement	None	Significant	None	Insignificant
Multinucleate Cells	None	Present	None	None
Cellular Debris	Minimal	Significant	Minimal	Minimal
Lipofusein	Low	High	Low	Low
Actin filaments	Diffuse	Highly Polymerized	Diffuse	Less Polymerized
Microturbules	Orderly	Disorganized	Orderly	Orderly

When propagated in the laboratory, normal human skin cells divide a predictable number of times and then die. These cells proliferate rapidly early on, then division rates slow. Finally the cells cease replicating. Cells in late passage are considered "old" cells and have been frequently used in comparative studies with "young" or early passage cells.⁵ A variety of alterations in cell morphology and other cell characteristics occur as the cells progress from young, vigorous cells to old, drying ones. In pioneering aging studies, Hayflick has proposed that the reduction in potential of human cultured fibroblasts to divide is a manifestation of aging at the cellular level.

In the recently published study, Kinetin delayed or prevented a range of cellular changes associated with *in vitro* aging of human skin cells, including alterations in cell morphology, growth rate, size, cytoskeletal organization, macromolecular synthetic activity and accumulation of lipofuscin aging pigments (Table 1).¹ One of the hallmarks of aging tissues is the accumulation of a variety of lipid-derived pigments called lipofuscins, the so-called "wear-and-tear" pigments. Kinetin-treated old cells appeared to be similar under the microscope to young cells; whereas, untreated old cells displayed marked morphological changes typical of cellular senescence.

Unlike a variety of previously tested agents that can alter certain features of cellular aging *in vitro*, Kinetin did not in this study alter the maximum *in vitro* life span of human skin cells or their ability to multiply in culture. Thus, Kinetin was devoid of activities associated with cellular immortalization, malignant transformation and carcinogenesis. These initial *in vitro* scientific data suggest that Kinetin appears possess a combination of effectiveness and safety in treating aging skin unmatched by other revitalizing skin treatments.

Moisturizers and Other Skin Care Programs

A class of products that won't cure (or prevent) wrinkles are the moisturizing creams and lotions. The beneficial effect of such cosmetics lasts no longer than several hours beyond their application and removal. Moisturizers improve the skin's appearance by hydrating (restoring and maintaining water) the stratum corneum; moisturizers have no effect on

the dermis. Some cosmetics contain agents that cause low-grade inflammation and give the appearance of decreasing wrinkles through subclinical swelling.⁷

Moisturizers generally are composed of water, oil and humectants.⁸ Humectants help the skin retain moisture, thereby making it more pliable and soft. Common humectants include glycerin, propylene glycol, pyrrolidone carboxylic acid, sodium lactate, urea, and certain natural lipid mixtures. More exotic humectants include certain proteins, gelatin, hyaluronic acid, vitamins and some natural ingredients. In general humectants act by penetrating into the stratum corneum and increasing the amount of moisture that is held in close association with the layer.⁹

Dry skin is characterized by the lack of moisture in the stratum corneum. Moisture originates in the lower skin and moves up through the stratum corneum, where it hydrates the cells and then evaporates into the atmosphere. The moisture content in the stratum corneum itself is dependent both on naturally occurring lipids and on intracellular water-soluble substances called natural moisturizing factors.⁸ In aging skin, natural moisturizing factors are only present in low amounts, and the water-binding capacity is reduced to about 75% of normal." Moreover, the sebaceous glands produce fewer lipids to replenish the natural supply, and wrinkles compound the problem by creating more surface area from which water can evaporate.

Yet, even though humectants temporarily increase the hydration state of the stratum corneum, they can actually eventually increase the skin's water loss by attracting water to the skin surface. This can lead to a perception of skin tightness or dryness.¹¹ Therefore, moisturizers also contain a class of substances, called occlusives, which coat the skin with an oil. Occlusives include substances like petrolatum, lanolin alcohol's, jojoba oil, cocoa butter, paraffin, cholesterol, heavy lipid mixtures, olive oil and heavy mineral oil. Moisturizers also contain emollients and lubricants that provide skin care products with the appropriate tactile feel and rub-in properties. These lotions smooth the roughened surface of the stratum corneum by filling the spaces between dry skin cells with oil droplets. Emollients can include a host of ingredients from silicone oils to cetyl alcohol's, cholesterol, mineral oil, silicone oils, vitamin E, some waxy esters and certain quaternary compounds.⁹

Collagen and elastin are added to a number of skin lotions, and it has been implied that they replace the old, worn out collagen or elastin in the skin, thus eliminating wrinkles. However, these extracts of protein are much too large to penetrate the stratum corneum. They merely dry to a protein film that fills in the irregularities of the skin surface and makes it appear smoother. Protein films shrink slightly on drying, thereby stretching out some of the fine wrinkles and surface irregularities for a short time. But this is purely a temporary, cosmetic change.¹¹ Liposomes, which have been marketed by the cosmetics industry since the mid 1980s, also have no permanent effect on the skin. They probably do not cross through the stratum corneum.¹² They are thought to coat the skin surface, causing humectant agents to remain on the skin longer.

1. Rattan SI, Clark BF: Kinetin delays the onset of aging characteristics in human fibroblasts. *Biochem biophys Res Commun* 1994; 201:665-72
2. Soriano-Garcia M, Parthasarathy R: Structure-activity relationship of cytokinins: crystal structure and conformation of 6-furfurylamino purine (kinetin), *Biochem Biophys Res Commun* 1975; 64:1062-8
3. West MID: The cellular and molecular biology of skin aging. *Arch Dermatol* 1994; 130:87-95
4. Kurban RS, Bhawan 1: Histologic changes in skin associated with aging. *J Dermatol Surg Oncol* 1990; 16:908-14.
5. Schneider EL In vitro skin fibroblast studies and human aging. In Balin AK, Kligman AM (eds), *Aging and the Skin*, Raven Press, New York, 1989, op 85-92.

6. Hayflick L Cell aging. In Eisdorfer C (ed), Annual Review of Gerontology and Geriatrics, vol 1, Springer Publishing, New York, 1980, pp 26-67.
7. Weiss JS, Ellis CN, Goldfarb MT, Voorhees JJ: Tretinoin treatment of photodamaged skin. Cosmesis through medical therapy. *Dermatol Clin* 1991;9:123-9
8. Ozawa T, Nishiyama S, Horii I, Kawakaki K, Tkahashi M, Kumano Y, Nakayama Y: Function of moisturizers and their roles in cutaneous aging. In Kligman AM, Takase Y (eds), *Cutaneous Aging*, University of Tokyo Press, Tokyo, 1988, pp 607-18.
9. Spencer TS: Dry skin and skin moisturizers. *Clin Cermatol* 1988;6:24-8.
10. Raab WP: The skin surface and stratum corneum. *Br I Dermatol* 1990;122 (Suppl 35):37-41.
11. Wehr RF, Krochmal L Considerations in selecting a moisturizer. *Cutis* 1987;39:512-5
12. Hope MI, Kitson CN: Liposomes: a perspective for dermatologists. *Dermatol Clin* 1993;