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Sponsored Symposium Highlights

Kinetin: Leading the Way to Healthy Skin

For over the past few decades the anti-aging properties of kinetin (Kinerase®), Invida have been explored extensively. At a sponsored symposium, held recently in Kuala Lumpur, Professor Suresh Rattan of Department of Molecular Biology and Genetics, Aarhus University, Denmark, discussed the mechanism of human aging and the biological effects of kinetin on the aging process.

Are we programmed to age?

Dramatic strides have been made in the field of medical interventions to reverse aging. The exact lifespan of an organism cannot be determined by specific genes. However, this does not imply that genes have no influence on survival, longevity and aging.¹ Biological aging starts when we live longer than our 'essential lifespan' as required by the evolution. The window of time needed to make a reproductive contribution to the next generation is known as essential lifespan.² Many factors affect aging and longevity of an individual, such as:

- Lifespan of parents and grandparents
- Woman's age at first child birth
- Level of education
- Social network (partner, children, siblings, friends)
- Self-perceived and socially-perceived age and health status.

Paradoxically, oxygen and food, which are essential for the existence of life, are also the main sources of damage in the body. Aging at the biological level is characterized by the progressive accumulation of molecular damage caused by free radicals, spontaneous errors in biochemical reactions and by nutritional components. The prevention of this damage may be achieved by improving the maintenance and repair systems.

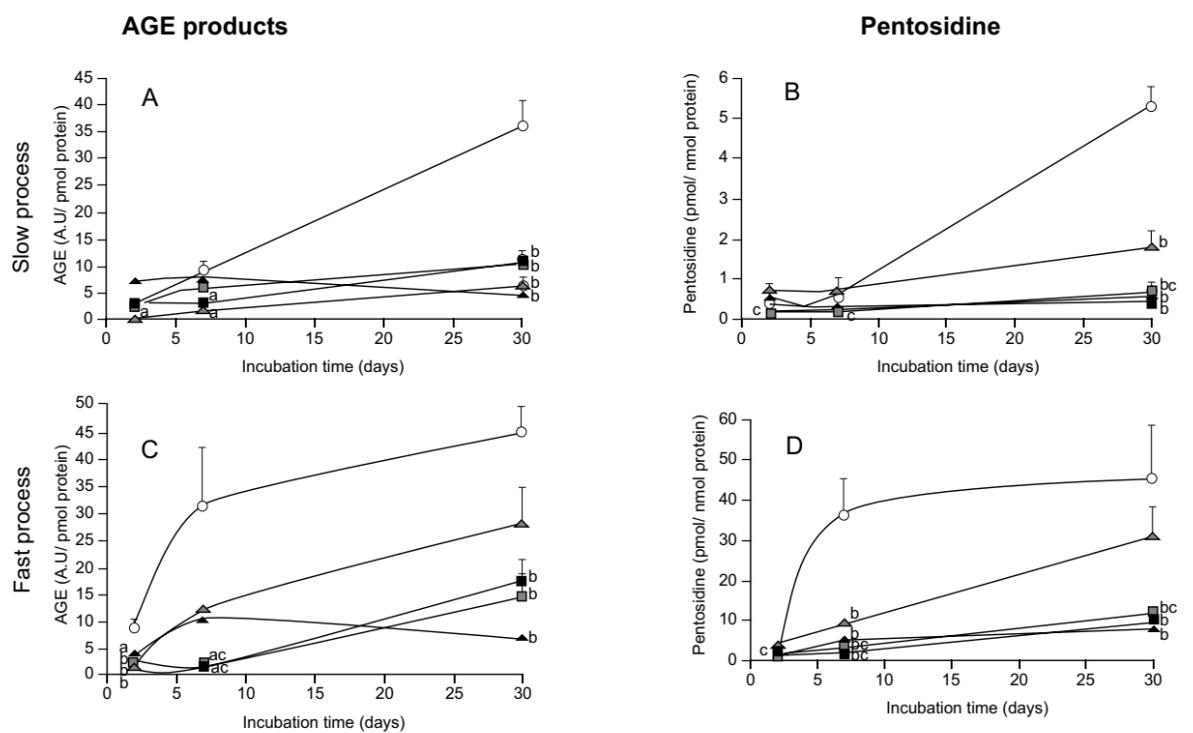
Kinetin delays the onset of aging in human fibroblasts

Kinetin (6-furfuryladenine) is a cytokinin growth factor that protects DNA and proteins from the free radical-induced damage. Until 1996, kinetin was thought to be an unnatural synthetic product. It was then found to be an intrinsic and naturally occurring modified adenine base. Kinetin has been detected in commercially available DNA, freshly extracted cellular DNA from human cells and in plant cell extracts. It is produced in cells as a result of protection against oxidative damage.³ Kinetin has been demonstrated to slow down aging, prolong lifespan and increase antioxidant defenses.

Experimental studies have reported its anti-aging action not only in plants, but also in human skin fibroblasts. Addition of kinetin to cultures of human fibroblasts was shown to prevent the accumulation of "wear-and-tear" pigments known as lipofuscin. Cells grown in the presence of kinetin maintained their youthful morphology for a much longer period, and stabilized the cytoskeleton. When kinetin was removed from the culture medium, some aging characteristics began to reappear in subsequent cell populations. It is important to note that kinetin is neither carcinogenic in terms of inducing any unnecessary cell proliferation nor toxic in terms of inducing cell death of normal human cells.^{4,5}

Skin changes are considered to be a marker for biological aging. The process of aging alters metabolism in fibroblasts reducing their lifespan, capacity to divide and produce collagen, resulting in diminished skin elasticity.⁶ Kinetin enhances and accelerates differentiation in human keratinocytes. It delays the onset of several cellular and biochemical characteristics associated with cellular aging, reduces melanin pigmentation and improves the structure of collagen and elastic fibers.⁷ Experimental evidence demonstrates that kinetin delays the aging of endothelial cells as well as increases cell proliferation and metabolic capacity.⁸ A similar cytokinin plant growth factor, zeatin, (6-[4-hydroxy-3-methyl-but-2-enylamino]adenine), which is present naturally in the RNA, has also been observed to have gerontomodulatory, youth preserving and anti-aging effects on serially passaged human adult skin fibroblasts undergoing aging.¹⁰

Figure 2: Kinetin inhibits protein oxidation and glycoxylation



BSA was incubated with either glucose (A, B) or ribose, arabinose, and glyoxal (C, D) alone (O) or in the presence of 50 μM (Δ) or 200 μM (▲) of adenine or 50 μM (□) or 200 μM (■) of kinetin. ^a p<0.05 vs. control without adenine and kinetin, ^b p<0.01 vs. control without adenine and kinetin, ^c p<0.05 vs. sample incubated with the same concentration of adenine.

Very recently, a study has revealed that a cosmetic formulation containing a dispersion of liposome with magnesium ascorbyl phosphate, alpha-lipoic acid and kinetin showed photo-protective effects in skin barrier function as well as pronounced hydration effects on human skin, which suggests that this dispersion has potential anti-aging effects.⁹ The results of a clinical trial showed beneficial effects of topical kinetin 0.1% lotion in reducing erythema and overall clinical scores in mild to moderate rosacea. At 12 weeks, 58.8% of the subjects showed moderate to marked improvement. Kinetin was well tolerated and also improved the skin texture and mottled hyperpigmentation associated with photodamage.¹¹

Possible mechanisms of kinetin

Although the exact mechanism of action of kinetin is still unclear, there are three main possible pathways suggested. Kinetin may physically interact with DNA, RNA and proteins to protect them from damage or directly neutralize damaging agents (Figure 1 and 2).^{12,13} It is possible that kinetin acts as

a signaling molecule and a stimulant of defense pathways, such as DNA repair and proteasome mediated protein turnover. Another possible mode of action is through its effects on the cell membrane and on the intracellular calcium flux.¹⁴ In summary, there are three possible mechanisms of actions of kinetin: direct removal of reactive oxygen species, direct binding with macromolecules, or indirect initiation of defense pathways.

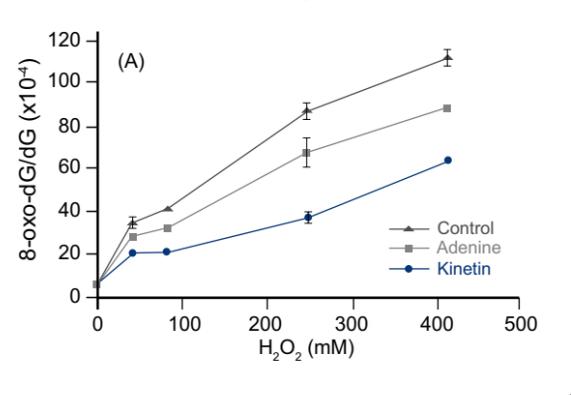
Externally supplied kinetin has pleiotropic beneficial effects

Kinetin has a wide range of beneficial effects. It may act as an aging modulator, lifespan enhancer, cell stimulator and melanin synthesis inhibitor. It possesses significant anti-thrombotic and anti-cancer properties. Furthermore, it plays an important role as a protector of DNA and proteins, from free radicals and glucose metabolites.¹⁵

Potential uses

Kinetin has great potential to be used as a nutritional supplement for stimulating the maintenance and repair pathways in the body. It plays a key role in hydration, protective and anti-aging, without causing irritation. Its uses need to be explored not only in the fields of cosmeceuticals and nutraceuticals, but in specialized treatment for certain genetic defects.

Figure 1: Kinetin protects DNA from free radical-induced damage



References: 1. Rattan SI. *EMBO Rep* 2005;6:S25-S29. 2. Rattan SI. *Free Radic Res* 2006;40:1230-1238. 3. Barciszewski J, et al. *FEBS Lett* 1996;393:197-200. 4. Sharma SP, et al. *Biochem Biophys Res Commun* 1995;216:1067-1071. 5. Rattan SIS, Clark BFC. *Biochem Biophys Res Commun* 1994;201:665-672. 6. Levakov A, et al. *Med Pregl* 2012;65:191-195. 7. Kimura T, Doi K. *Rejuvenation Res* 2004;7:32-39. 8. Lee JH, et al. *Proteomics* 2006;6:1351-1361. 9. Campos PM, et al. *Photochem Photobiol* 2012;88:748-752. 10. Rattan SI, Sodagam L. *Rejuvenation Res* 2005;8:46-57. 11. Wu JJ, et al. *Clin Exp Dermatol* 2007;32:693-695. 12. Olsen A, et al. *Biochem Biophys Res Commun* 1999;265(2):499-502. 13. Verbeke P, et al. *Biochem Biophys Res Commun* 2000;276(3):1265-1270. 14. Barciszewski J, et al. *Plant Sci* 1999;148:37-45. 15. Rattan SI. *Hum Exp Toxicol* 2008;27:151-154.

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