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COSMECEUTICALS FROM PHARMACEUTICAL AIDS

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ABSTRACT

Aging of the skin is the result of continuous "wear and tear" processes, which in turn damages the cellular DNA and proteins. Wrinkles are one of the most difficult sings of aging. Aging of the skin involves degradation of the extra cellular matrix, which can be characterized by many factors such as uneven pigmentation, laxity and wrinkles. It is also found that an aged skin shows decreased collagen levels, looses its proliferation capacity and moisture content. Luckily, to combat this aging process, the nature has provided us several natural ingredients that help our skin to look young and supple. This review discusses about 3 biopolymers namely the Collagen, Chitosan and *Aloe vera* which are individually found to possess anti-aging properties. Owing to their anti-aging properties, it is proposed that these 3 biopolymers can be used as a common ingredient in anti-aging formulations.

INTRODUCTION

Skin is the largest organ in our body and its appearance conveys one's health, lifestyle and overall well being of a person [1]. Aging of the skin is the result of continuous "wear and tear" processes which in turn damages the cellular DNA and proteins [2]. Aging skin can be characterized by many factors such as uneven pigmentation, laxity and wrinkles. The facial aging process involves simultaneously 3 layers namely the epidermis, dermis and the subcutaneous tissues. Also the solar radiation is found to accelerate the body's natural aging process by various mechanisms. The mechanisms of skin aging can be divided into 2 groups namely the intrinsic aging, which is the natural or chronologic aging of skin and the extrinsic aging, which is influenced by physical and chemical factors. In case of extrinsic facial aging, the solar radiation is found to be the major contributor because of extensive cumulative exposure to UV radiation over one's lifetime.

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However the intrinsic or natural mechanism is also found to play a role in the way an individual ages, and thus both the intrinsic and the extrinsic mechanisms share the molecular pathways in aging [3].

Characterization of Natural and Photoaging

Natural aging can be characterized by fine wrinkles and a crepe like quality of the skin, being seen in its purest form on sun protected sites such as the upper, inner arm. In case of sun exposed sites or face, it is seen in conjunction with photo aged skin [4]. Whereas photo aging is characterized by wrinkles, redness, dyspigmentation and is seen on the sun exposed sites such as the face, posterior neck and forearms [5]. Therefore there exists a fairly clear sequence of events that commences with UV light exposure and culminates with collagen fragmentation, finally leading to an aged appearance.

In photo aged skin, fragmented collagen fibres and fibroblast in a collapsed state exists, thereby unable to attach to the collagen network. Also the collagen is found to be decreased by 70% and collagenase levels are increased about 4 fold [6]. Thus in an aging skin collagen levels are decreased and also the cell looses its

proliferation capacity and moisture content.

This review discusses about a composite prepared using 3 biopolymers namely Collagen, Chitosan and *Aloe vera* which in turn helps to overcome a sagging dry skin. Also in a study *Aloe vera* blended collagen Chitosan composite as a scaffold has already been found to possess all requisite physical and biological properties to recruit, attach and proliferate the fibroblasts. Therefore, on considering the overall physico chemical and biological properties of the *Aloe vera* blended Collagen - Chitosan as a scaffold, it is proved as a promising biomaterial for tissue engineering [7]. The purpose of this article is to review the anti-aging properties of Collagen, Chitosan and *Aloe vera.*

Collagen

Collagen is a well known protein and is widely used in medical applications. Among the natural polymers and their synthetic analogues used as biomaterials, the characteristics of collagen are distinct mainly in its mode of interaction in the body [8]. When compared to other natural polymers such as the albumin, gelatin, collagen etc., the most preferred is the collagen as it exhibits biodegradability, weak antigenicity and in addition, it is known for superior biocompatibility due to is low toxicity and poor immunogenic reactions which is found to be the main criteria for selecting collagen as a biopolymer in this study. Collagen, a major structural protein of extra cellular matrix supports the growth of a wide variety of tissues, which its structure imparts favorable properties such as mechanical strength [9]. These properties help in exploiting this biodegradable polymer is anti-aging formulations. Approximately 30% of all vertebrate body protein is constituted by the structural protein collagen. The extra cellular protein of the tendon and bone are constituted by more than 90% of collagen while the skin is constituted by more than 50% of collagen [10]. The ubiquitous biodegradable collagen constitutes a family of genetically distinct molecules and possesses a unique triple helix configuration of 3 polypeptide sub units known in common as α-chains. Currently atleast 13 types of collagen, varying in length of the helix, nature and in the size of non-helical portions have been isolated [11,12]. The types of collagen and its chain composition with their body distribution is tabulated as [12].

As, this review discusses about an anti-aging formulation it is important to focus on the proliferative activity of the cells present in the skin. Also, it is speculated that collagens of particularly type I, found predominantly in skin of higher order animals [12] is by far the most abundantly used biomaterial in medical implants which can support the growth of different cell types [13]. Therefore, the discussion on anti-aging will be limited to type I collagen. Despite of being accepted as a safe and multifunctional material [14,15], the collagen being an animal derived biopolymer will raise concerns regarding its potential to evoke immune responses [16].

Also, collagen is considered to be a weak antigen, despite of its subsequent evidence demonstrating its ability to interact with antibodies [15,17]. It was found that antigenicity can be suppressed by removal of the non helical component from the collagen. [18,19]. On the other hand, chemical cross linking with substances such as glutaraldehyde tends to reduce antigenicity but cannot eliminate it completely [20,21].

Collagen – Best Biopolymer in Anti-aging Formulations

The primary reason for using collagen in biomedical field is that it can form fibres with extra strength and stability through its self-aggregation and cross-linking [22]. Collagen shows very low antigenicity and also exhibits an easy absorption in the body. In addition, it possesses high tensile strength and high affinity with water. In addition, it exhibits non-toxic, bio-compatible and biodegradable properties [23,24]. Collagen can also be prepared in a number of different forms such as strips, sheets, sponges and beads.

Solubilization of collagen in an aqueous solution, particularly in acidic aqueous media is possible and it can also be engineered to exhibit tailor-made properties. As collagen functions as the primary structural protein in the body, it is relatively stable but it is still liable to collagenolytic degradation by enzymes, such as collagenase and telopeptide cleaning enzymes [25]. Following plastic surgery using Collgen implants and wound breakdown using catgut suture material, adverse reactions have been reported, found restricted to localized redness and swelling [26].

Chitosan

Chitosan, a natural polysaccharide, consists of β (1-4) linked D- glucosamine residues with a variable number of randomly located N-acetyl glucosamine groups [27]. The Chitosan polymer is charged positively because of the presence of amino groups and solubilized by protonation at environmental pH values of < 6. Therefore the degree of deacetylation influences the solubility of Chitosan. Also, cross linking helps in improving the mechanical properties of Chitosan [28]. Many studies have indicated that the Chitosan exhibits a variety of biological properties and consequently, different applications for these biopolymers have been found in various fields such as agriculture, industry and recently in the medical field as well (29,30). In addition its other characteristics such as non-toxicity, biocompatibility and biodegradability, allows Chitosan to be used also as film, gel or solution [31].

Among the naturally derived polymers special attention have been given to collagen [32-34] and Chitosan [35-37], because of their biological and chemical similarities with natural tissues. However, the ability of Chitosan to induce local cell proliferation and its ability to be stable enough when integrated with the host tissue makes it as an attractive alternative [38].

Chitosan as a Biopolymer in Anti-aging Formulation

Inspite of chitosan being non-cytotoxic, it may inhibit fibroblast proliferation [39]. Though Chitosan is unsuitable for invitro fibroblasts cultivation, its use is still suggested in combination with other materials [40]. Further, it has been reported that the Chitosan incorporated into a collagen scaffold is known to increase its mechanical strength, as it forms an ionic complex between the positively charged Chitosan and the negatively charged collagen [41]. In addition many studies indicated that scaffolds composed of collagen and Chitosan may result in an appropriate environment for the regeneration of skin. Though many studies have shown that the skin fibroblasts are not very compatible with Chitosan the addition of collagen has been reported to facilitate the attachment and proliferation of skin fibroblasts.

Aloe vera

Nowadays, number of skin lotions, sun blocks and cosmetics use Aloe-vera as an active ingredient [42]. *Aloe vera* is botanically named as *Aloe barbadensis* miller, belonging to the Asphodelaceae (Liliaceae) family. The plant bears long (upto 20 inches long and 5 inches wide), triangular and fleshy leaves with spikes along the edges. The center of the leaf has clear and fresh parenchymal gel, which is sometimes dried to form *Aloe vera* concentrate or is diluted with water to create aloe juice products. The leaf (rind) is then lined with yellowish green pericyclic tubules from which sticky latex liquid is derived [43].

Active constituents of the *Aloe vera* gel

The gel consists of (i) polysaccharides such as glucomannan and acemannan (ii) other active constituents of the gel includes carboxy peptidase, magnesium, zinc, calcium, glucose, cholesterol, salicylic acid, prostaglandins, precursors [gamma linolenic acid (GLA)], vitamins A,C,E, lignins, saponins, plant sterols and amino acids [51].

***Aloe vera* gel in Antiaging Formulations**

The raw pulp of *Aloe vera* comprises approximately about 98.5% water, while the mucilage on gel contains 99.5% water [44]. This high water content present in the aloe gel combats aging and mobilizes the skin to appear younger and more radiant. As the gel has similar anti-aging effects as that of vitamins A derivatives, its use in cosmetics has been boosted by claims [45]. The gel contains an emollient polysaccharide named glucomannan which acts as a good moisturizes and is therefore accounted for its use in many cosmetics [46]. The gel has an activity of stimulating cell growth and as such also enhances the property of restoring the damaged skin. It is said to moisturize the skin because of its water holding capacity [47].

Aloe produces collagen and elastin fibres by stimulating the fibroblasts production there by in turn making the skin more elastic and less wrinkled. Aloe is also reported to have cohesive effects on the super facial flaking epidermal cells by sticking them together, thereby softening the skin. In addition, the amino acids present in the aloe gel helps in softening the hardened skin cells and zinc tightens the pores by its astringent property. The moisturizing activity of aloe gel have been studied in the treatment of dry skin associated with occupational exposure, where Aloe-vera gel gloves enhanced the integrity of the skin, decreased the appearance of fine wrinkles and also decreased erythema [48]. In addition, it has antiacne effects [49].

Table 1. Types of Collagen and its Chain Composition with their Body Distribution

Collagen Types	Chain composition	Tissue distribution
I	(α1(I))2 α2(I), trimer (α 1(I))3	Skin, tendon, bone, cornea, dentin, fibrocartilage, large vessels, intestine, uterus, dentin, dermis, tendon
II	(α1(II))3	Hyaline cartilage, vitreous, nucleus pulposus, notochord
III	(α1(III))3	Large vessels, uterine wall, dermis, intestine, heart valve, gingiva
IV	(α1(IV))2 α2(IV)	Basement membranes
V	α1(V) α2(V)(3(V) or (α1(V))2 α2(V) or (a1(V))3	Cornea, placental membranes, bone, large vessels, hyaline cartilage. Gingival
VI	α1(VI) α2(VI) α3(VI)	Descemet's membrane, skin, nucleus pulposus, heart muscle
VII	(α1(VII))3	Skin, placenta, lung, cartilage, cornea
VIII	α1(VIII) α2(VIII) chain organization of helix unknown	Produced by endothelial cells, Descemet's membrane
IX	α1(IX) α2(IX) α3(IX)	Cartilage
X	(α1(X))3	Hypertrophic and mineralizing cartilage
XI	1 α2a3 α1 or α1(XI) α2(XI) α3(XI)	Cartilage, intervertebral disc, vitreous humour
XII	(α1(XII))3	Chicken embryo tendon, bovine periodontal ligament.
XIII	Unknown	Cetal skin, bone, intestinal mucosa.

CONCLUSION

An aged skin shows decreased collagen levels, decreased moisture content, decreased cell proliferation activity with increased free radical release. As this review individually enlightens the anti aging properties of Collagen, Chitosan and *Aloe vera* which when applied topically helps to increase the decreased collagen level, increases the cell proliferation capacity and also retains the moisture content of the skin. These 3 biopolymers can be used as a common ingredient in anti aging formulations.

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REFERENCES

1. Dana S, Yolanda H, John V. (2009). Molecular Mechanisms in skin Aging. *Cosmet Dermatol*, 22, 291-295.
2. Hashizume H. (2004). Skin Aging and Dry Skin. *Dermatol*, 31(8), 603-609.
3. Andrea TM, Kathryn GK, Erin EB. (2012). Mechanisms of Skin Aging. *Cosmet Dermatol*, 25, 399-402.
4. Varani J, Dame MK, Rittie L, (2006). Decreased Collagen Production in Chronologically Aged Skin, Roles of Age – Dependent Alteration in Fibroblast function and Defective Mechanical Stimulation. *Am J Pathol*, 168, 1861-1868.
5. Varani J, Perone P, Fligiel SE. (2002). Inhibition of type I Procollagen Production in Photodamage, Correlation Between Presence of High Molecular Weight Collagen Fragments and Reduced Procollagen Synthesis. *J Invest Dermatol*, 119, 122-129.
6. Fisher GJ, Varani J, Vorhees JJ. (2008). Looking older, Fibroblast Collapse and Therapeutic Implications. *Arch Dermatol*, 144, 666-672.
7. Panneerselvam J, Abraham M R, Thamiran K, Asit B Ml, Chellan R. (2013). Preparation and Characterization of *Aloe vera* Blended Collagen- Chitosan Composite Scaffold for Tissue Engineering Applications. ACS Appl Mater Interfaces, 5, 7291-7298.
8. McPherson JM, Sawamura S, Amstrong R. (1986). An Examination of the Biologic response to Injectable, Glutaraldehyde Cross-linked Collagen Implants. *J Biomed Mater Res*, 20, 93-107.
9. Nimni ME, Cheung D, Strates B, Kodama M, Sheikh K. (1987). Chemically modified Collagen, a Natural Biomaterial for Tissue Replacement. *J Biomed Mater Res*, 21, 741-71.
10. Piez KA. (1985). Collagen, in, J.I. Kroschwitz (Ed.) Encyclopedia of Polymer Science and Engineering, Wiley, New York, 699-727.
11. Kucharz EJ. (1992). The Collagens, Biochemistry and Pathophysiology, Springer- Verlag, Berlin, 7-29.
12. Miller EJ. (1988). Collagen types, Structure, Distribution and Functions, in, M.E. Nimni (Ed.), Collagen Vol. I-Biochemistry, CRC Press, Boca Raton, FL. 139-157.
13. Kleinman HK, Klebe RJ, Martin GR. (1981). Role of Collagenous Matrices in the Adhesion and Growth of Cells. *Journal of Cell Biology*, 88, 473-485.
14. Li ST. (1995). Biologic biomaterials, Tissue-derived Biomaterials (Collagen). In, Brozino JD, editor. The Biomaterial Engineering Handbook. Boca Raton, FL, CRC Press, 627-647.
15. Gorham SD. (1991). Collagen. In, Byrom D, editor. Biomaterials NewYork, Stockton Press, 55-122.
16. Crumpton MJ. (1974). Protein antigens, The Molecular Basis of Antigenicity and Immunogenicity. In, Sela M, Editor. The Antigens. New York, Academic Press, 1-78.
17. Furthmayur F, Timpl R. (1976). Immunochemistry of Collagens and Procollagens. *Int Rev Connect Tissue Res*, 7, 61-99.
18. Chvapil RL, Kronentahl W, Van Winkle JR. (1973). Medical and surgical applications of collagen, in, D.A. Hall, D.S. Jackson (Eds.), International Review of Connective Tissue Research, Academic Press, New York, 1-61.
19. Knapp TR, Luck E, Daniels JR. (1977). Behaviour of Solubilised Collagen as a Bioimplant. *J Surg Res*, 23, 96-105.
20. DeLustro F, Condell RA, Nguyen MR, McPherson JM. (1986). A Comparative Study of the Biologic and Immunologic Response to medical devices derived from Dermal Collagen. *J Biomed Mater Res*, 20, 109-120.
21. Meade KR, Silver FH. (1990). Immunogenicity of Collagenous Implants. *Biomaterials*, 11, 176- 180.
22. Barbani N, Giusti P, Lazzeri L, Polacco G, Pizzirani G. (1995). Bioartificial Materials Based on Collagen (Mr 5000) Increases update into liver. *Biochim Biophys Acta*, 1279, 259-265.
23. Friess W. (1998). Collagen- Biomaterial for Drug Delivery. *Eur J Pharm Biopharm*, 45, 113-136.
24. Maeda M, Tani S, Sano A, Fujioka K. (1999). Microstructure and Release Characteristics of the Minipellet, a Collagen Based Drug Delivery System for Controlled Release of Protein Drugs. *J Controlled Rel*, 62, 313-324.
25. Wooley DE. (1984). Mammalian Collagenases. In, Piez, K.A., Reddi, A.H. (Eds.), Extracellular Matrix Biochemistry. *Elsevier*, New York, 119-158.
26. Webster RC, Kattner MD, Smith RC. (1984). Injectable Collagen for Augmentation of Facial Areas. *Arch Otolaryngol*, 110, 652-656.
27. Francis Suh JK, Howard WT. (2000). Application of Chitosan- Based Polysaccharide Biomaterials in Cartilage Tissue

Engineering, A Review. *Biomaterials*. 21, 2589-2598.
28. Senel S, Ikinci G, Kas S, Yousefi Rad A, Sargon MF, Hincal AA. (2000). Chitosan Films and Hydrogels of Chlorhexidine Gluconate for Oral Mucosal Delivery. *Int J Pharm*, 193, 197-203.
29. Singla AK, Chawla M. (2001). Chitosan, Some Pharmaceutical and Biological Aspects- An Update. *J Pharm Pharmacol*, 53, 1047-1067.
30. Park YJ, Lee YM, Lee JY, Scol YJ, Chung CP, Lee SJ. (2000). Controlled Release of Platelet- Derived Growth Factor- BB from Chondroitin Sulfate- Chitosan Sponge for Guided Bone Regeneration. *J Control Release*, 67, 385-394.
31. Badylak SF. (2004). Xenogeneic Extracellular Matrix as a Scaffold for Tissue Reconstrction. *Transpl Immunol*, 12, 367-77.
32. Gomathi K, Gopinath D, Rafiuddin AM, Jayakumar R. (2003). Quercetin Incorporated Collagen Matrices for Dermal Wound Healing Process in Rat. *Biomaterials*, 24, 2767-72.
33. Ruszczakz. (2003). Effect of Collagen Matrices on Dermal Wound Healing. *Adv Drug Deliv Rev*, 55, 1595-611.
34. Azad AK, Sermsinthan N, Chandrkrachang S, Stevens WF. (2004). Chitosan Membrane as a Wound- Healing Dressing, Characterization and Clinical Application. *J Biomed Mater Res*, 15, 216-22.
35. Mohy Eldin MS, Soliman EA, Hashem AI, Tamer TM. (2008). Chitosan Modified Membrane for Wound Dressing Applications, Preparations, Characterization and Bio-evaluation. *Trends Biomater Artif Organs*, 22, 158-68.
36. Jayakumar R, Prabaharan M, Sudheesh Kumar PT, Nair SV, Tamura H. (2011). Biomaterials Based on Chitin and Chitosan in Wound Dressing Applications. *Biotechnol Adv*, 29, 322-37.
37. Suh JK, Mathew HW. (2000). Application of Chitosan- Based Polysaccharide Biomaterials in Cartilage Tissue Engineering. A Review. *Biomaterials*, 21, 2589-98.
38. Chatelet C, Damour O, Domard A. (2001). Influence of the Degree of Acetylation on Some Biological Properties of Chitosan Films. *Biomaterials*, 22, 261-8.
39. Shahabeddin L, Damour O, Berthod F, Rousselle P, Saitigny G, Collombel C. (1991). Reconstructed Skin from Co-cultured Human Keratinocytes and Fibroblasts on a Chitosan Crosslinked Collagen- GAG Matrix. *J Mater Sci Mater Med*, 2, 222-6.
40. Taravel MN, Domard A. (1996). Collagen and its Interactions with Chitosan, III, Some Biological and Mechanical Properties. *Biomaterials*, 17, 451-455.
41. Grindlay D, Reynolds T. (1986). The *Aloe vera* Phenomenon, a Review of the Properties and Modern Uses of the Leaf Parenchyma Gel. *J Ethnopharmacol*, 16, 117-51.
42. Schulz V, Hanselk R, Tyler VE. (1997). Rational Physiotherapy, A Physicians Guide to Herbal Medicine. Berlin, Springer, 306.
43. Atherton P. (1998). Aloe vera, Magic or Medicine? *Nurs Stand*, 12, 49-52, 54.
44. Eshun K, He Q. (2004). Aloe vera, A Valuable Ingredient for the Food, Pharmaceutical and Cosmetic Industries- A Review. *Crit Rev Food Sci Nutr*, 44, 91-96.
45. Danhof I. (1993). Potential Reversal of Chronological and Photo-aging of the Skin by Topical Application of Natural Substances. *Phytotherapy Research*, 7, S 53-56.
46. Henry R. (1979). An Updated Review of Aloe vera. *Cosmetics and Toiletries*, 94, 42-50.
47. Morton JF, Folk Use and Commercial Exploitation of Aloe Leaf Pulp. *Economic Botony*, 15, 311-319.
48. West DP, Zhu YF. (2003). Evaluation of *Aloe vera* Gel Gloves in the Treatment of Dry Skin Associated with Occupational Exposure. *Am J Infect Control*, 31, 40-2.
49. Surjushe A, Vasani R, Saple DG. (2008). Aloe vera, A Short Review. *Indian Journal of Dermatology*, 53, 163-6.