July 17, 2003

ALOE VERA – A REVIEW OF THE SCIENTIFIC LITERATURE.

Aloe Vera and the ageing process – its relation to glycation and glycosylation

This article reviews the current scientific research literature regarding Aloe Vera, its uses and place in health and wellbeing. The literature reviewed covers in vivo and in vitro, human and animal, studies. Special attention is given to the question – does Aloe Vera, in particular one of its polysaccharides mannose (mannose-6-phosphate) contribute to or cause glycation? Additional topics covered: glycation and its causational factors; the safety of long-term Aloe Vera use, internal and topical. pages 1-9

GLYCATION

Glycation or non-enzymatic glycosylation is defined as the chemical reaction between reducing sugars, (glucose, fructose, etc) and free protein amino acids. This non-enzymatic modification of tissue protein amino acids by reducing sugars is know as the Maillard or browning reaction.[1] This results in cross-linking, and the subsequent formation of reversible Amadori products. With sufficient time, the Amadori products "spontaneously undergo further crosslinking to form irreversible crosslinks called advanced glycation endproducts (AGEs)".[2] As a result the protein amino acids are altered in structure and function.[3]

In short, glycation is the inevitable "sugar-processing", where sugar irreversibly attaches to long-lived proteins such as collagen, accumulating with age. This leads to the destructive (abnormal) cross-linking of the structural proteins of tissues and organs. The result is stiffening; decreased flexibility and elasticity (hardening) of the organs and tissues made up of these protein amino acids. This causes a gradual deterioration of normal tissue and organ functioning - repair, defense and coping mechanisms.

Glycation is associated with both intrinsic (internal, within the tissue itself) and actinic (due to radiation by which chemical effects are produced) ageing. AGEs are associated with cellular dysfunction, age-related diseases and conditions.[4] Besides normal aging, glycation is also associated with a wide variety of conditions and diseases such as hypertension, diabetes, cancer, arthrosclerosis, general cardiovascular disease and Alzheimer to name but a few.

Conditions for glycation and the formation of AGEs must be correct however. These reactions take a long time to occur and only proteins with significant amounts of the Amadori products present will accumulate substantial amounts of AGEs.[5] This occurs on long lived proteins (i.e. tissues with low turnover rate) (i.e. fibronectin, laminin, collagen, elastin, etc) [6], when high concentrations of sugar are present, as with diabetes mellitus.[7]

FACTORS – *causes of glycation*

The factors influencing glycation and its acceleration are: age, solar (UV) radiation, the amount of caloric intake, tissue type, level of reducing sugars present, smoking of tobacco, oxidative stress, general health and metal ions.

Age – because glycation influences long-lived proteins, it has been determined that with advancing years (ageing), the accumulation of AGEs increases. In the human dermis after 35, glycation arises and increases with intrinsic ageing.[8]

Solar (UV) radiation – AGEs when exposed to ultra violet light (UV) A, natural or artificial source, generate reactive oxygen species (ROS). These promote photo-ageing in the skin.[9] Exposure to UV radiation increases dermal glycation.[10] Another reason why adequate sun protection and taking care when outside or exposed to sources of UV (by office lighting, thru windows, suntan beds, etc) is a must.

Amount of Caloric Intake – "age-related accumulation of AGE is more closely related to [the amount of] caloric intake …than a specific dietary carbohydrate" present in the diet.[11] The collagen concentrations of pentosidine, a tissue marker of AGE, are not affected significantly by the type of dietary carbohydrate (mono- or disaccharides) [12]. "Specific dietary carbohydrates do not affect the aging process by altering serum glucose concentrations or the accumulation of AGE in specific tissues."[12] The restriction of caloric intake has a beneficial effect in helping to delay the physiological effects of ageing.[12]

Tissue Type – different tissue types are susceptible to glycation and the accumulation of AGEs at different rates[12]. This difference may be due to the different types of long-lived protein amino acids present in the specific tissue. This may also be due to the differences in the levels of arginine and lysine in the specific tissue and their decrease with age.[13] For example, human cartilage collagen, with age, shows greater glycation than human skin, which in turn shows higher levels of glycation than human lens proteins.[14]

Presence of reducing sugars – the greater the presence of reducing sugars (i.e. the greater the caloric intake), the greater the prevalence of glycation. The greater the caloric intake, the higher the levels of serum glucose, thus the greater the availability for glycation.[15] *(see note A)*

Smoking of tobacco – a study from 2002 found that nornicotine, obtained from smoking tobacco, "causes aberrant [exceptional, abnormal] protein glycation."[16] A direct link between tobacco use and AGE development was reported. The research data suggests, "nornicotine-based glycation products could serve as long-lived sources of 'nicotine-like' moieties [parts], contributing to the mechanism of nicotine addiction."[17] Nornicotine could also lead to protein inactivation and cause adverse immune system responses.[17] This may be the reason why the skin around the mouth of a smoker will show the signs of ageing - hardening of the skin, lines and discoloration – much earlier and more prominently than the skin of a nonsmoker.

Oxidative stress – leads to the creation of free radicals, which in turn promotes the conditions for glycation.[17a]

General health – of the body is another important factor. Specific diseases, such as diabetes mellitus, immune stress and other health compromising conditions can increase the rate and severity of glycation.[18] The increase in glycation in these conditions and diseases in turn can result in additional complications and conditions or the worsening of the disease itself.

Metal ions - Glycation is also believed to occur as a result of the autoxidation of glucose in the presence of transition metal ions.[19] The rate of glycation is dependent upon the concentration of metal ions present, the final amount of the glycation, however, is not affected.[20] Thus ions from metals such as Iron (Fe) and Copper (Cu) increase the speed of glycation, not the degree.

Cooking of Foods at high temperatures – foods cooked at high temperatures exhibit higher levels of AGE formation.

ALOE VERA

Aloe Vera has enjoyed a reputation as a healer for millennia, based primarily on anecdotal evidence. For the last 40 years however, a concerted effort by the scientific research community, through in vivo (real life) and in vitro (within an artificial environment) studies (human and animal) has shed new light on Aloe Vera and its abilities. It has brought Aloe Vera out of the realm of folk medicine, providing it with a solid medical and scientific foundation as a healer.

Aloe Vera's numerous and varied constituent have provided this botanical with multi-faceted abilities, uses and applications.

Aloe Vera has been shown to assist in or with:

- ***pain management*** – through the inhibition of pain producing substances such as bradykinin and thromboxane [21]
- ***increase of blood circulation***, vasodilation - in wound and tissue injuries [21]
- ***minimization of bruising*** – by speeding the repair process and stimulating drainage.
- ***immunostimulation*** – the stimulation of the immune system, general and target-specific, by natural killer cell activity stimulation, due to the abundance of polysaccharides found in Aloe Vera [21] (activity found in patients with cancer, AIDS, tumors, to name but a few)
- ***antibacterial activity*** – demonstrates antibiotic properties [21]
- ***antiviral activity*** – found in patients with herpes simplex, measles, feline rhinotracheitis, feline leukemia, to name but a few – increases cell viability and reduces viral load, assisting in inhibiting glycosylation of viral glycoproteins, inhibiting virus-induced cell fusion, suppressing virus release, helping to disrupt the coating or enveloped viruses such as herpes and influenza virus A [21]
- ***antifungal activity*** [21]
- ***antioxidant activity*** [21]
- ***aspirin-like effect*** – due to the presence of salicylates [21]
- ***stimulation of cell proliferation and differentiation*** [21, 24a] (in a controlled manner)[24a]
- ***anti-inflammatory properties*** – speeding the healing process - wound & other injuries [21] - assisting in scar minimization [21]

- ***assistance with, reduction in or prevention of inflammatory conditions*** - such as adjuvant- induced arthritis [21, 21a]
- ***wound and burn healing*** – wide range of tissue injuries, including frostbite [21]
- ***carrier action*** – assisting other actives to perform better and more efficiently, often at reduced dosage [21]
- ***bio-availability enhancement*** – improves the absorption and efficacy of actives, with note both water and lipid(fat) soluble vitamins, especially vitamins C and E.[33] (see note D)
- ***anti-tumor activity*** – stimulating immune system response against tumors [21]
- ***yeast control*** – by stimulating immune system response against yeast infection [21]
- ***gastrointestinal dysfunction*** – decreasing bowel putrefaction, reducing transit time in the intestines, encouraging the increase of beneficial bacterial flora in the digestive tract, improving protein digestion and absorption [21]
- ***peptic ulsers*** [21]
- ***oral ulsers*** (aphthous stomatitis) – accelerated healing and reduced pain [21]
- ***anti-diabetic activity*** – reduces blood sugar levels (hypoglaecemic effect) [21]
- ***anti-cancer activity*** – through immune system stimulation (with note T-cell activation) [21]
- ***moisturization properties*** – actually more properly called hydrating properties, by bringing moisture deep into the skin
- ***UV radiation and burn treatment*** [21]

The list of the beneficial uses of Aloe Vera continues to grow, as more scientific research is performed.

Sometimes the research results are contradictory, one study reporting no results, while other studies report fantastic results. This may be attributed to a variety of factors:

1. the quality of the Aloe Vera used
2. the method of Aloe Vera cultivation
3. the location of cultivation
4. the handling of the Aloe Vera immediately following harvesting
5. the method of stabilization of the Aloe Vera
6. the method of processing
7. what parts of the Aloe Vera are used
8. what is removed from the Aloe Vera during processing

The most bioactive Aloe Vera is cultivated in those areas of the world which have arid conditions, offering the plant enough, yet infrequent, water. The correct amount of water is important, as it influences the amount and quality of the actives, particularly the polysaccharides, present upon harvest. Too much water causes the polysaccharide count to decrease. Water from natural sources (i.e. rain streams and rivers) is better than artificial irrigation.

The actives in any botanical are fragile, and Aloe Vera is no exception. This is why it is important that the Aloe Vera be promptly and properly handled immediately following harvest. A delay in stabilization and processing will deteriorate the quality and efficacy of the constituents.

Aloe Vera is notoriously difficult to stabilize, many methods have been tried, but if not done properly, the product will quickly deteriorate - active botanicals, such as Aloe Vera, require stabilization to preserve the actives (phyto-nutrients). Not unlike freshly squeezed fruit juice which if not immediately consumed or preserved will oxidize, causing it to lose all beneficial activity and become just like sugar 'water'.

The method of processing is also of crucial importance. Chemical processing or leaching, the most common method (to remove certain undesirable constituents - namely aloin and aloe emodin, known skin irritants) can lead to the introduction of substances, which can reduce the potency and efficacy of the Aloe Vera or cause adverse reactions. Chemical processing can also degrade or adversely affect the actives' content, integrity and activity. The more labor-intensive and expensive membrane-based mechanical filtration process is the superior method.

Furthermore, the traditional heating or pasteurizing of Aloe Vera places great stress on its constituents and compromise their structure and activity. Heating denatures the amino acids, deactivates the enzymes and breaks the lengths of the polysaccharide chains (the longer the polysaccharide chain, the greater its ability to stimulate the immune system). For these reasons, Cold Processing is the superior method to ensure and protect the activity and integrity of Aloe Vera's constituents.

In throwing away the rind or outer portions of the Aloe Vera leaf and using only the gel or matrix, which is standard practice in the industry, the vast majority of active constituents of Aloe Vera are also thrown away. It is estimated that 80 – 85% of the actives in Aloe Vera are found just underneath the surface of the rind (not unlike apples where the majority of the

vitamins and minerals are found just underneath the skin).

The medical and research community is beginning to realize that in the case of Aloe Vera, the whole is greater than the sum of its parts.

> "There may indeed be synergies which would not appear if the fractions [separate actives isolated from Aloe Vera] were kept separate." [21]
>
> "One feature that is becoming clear is that the systems undergoing healing contain several interacting factors, each of which may be affected by more than one component of the raw gel." [21]
>
> "Recognizing the possible multifarious activities of Aloe constituents, a series of tests of aloe gel on heat burns, electrical burns and frostbite in guinea pigs, rabbits and in clinical studies with humans demonstrated a therapeutic potential across the wide variety of soft tissue injuries." [21]
>
> "…the gel may have more than one active constituent, which may be addressing different parts of the healing process." [21]
>
> "The healing effects of A. vera gel are therefore now being seen as more complex than previously realized. It now appears that several activities are operating each with its own part to play in the overall therapy." [21]

The isolation of the constituents has given the scientific research community a basis of understanding regarding the individual roles and activities of these components. It is becoming evident, however, that there is a great deal more involved. The constituents of Aloe Vera function in concert; although each may perform an individual function or functions, it is the synergy of these functions and the resultant activity, which produces the beneficial results. Aloe Vera affords a holistic approach. (This can be compared to the scientific knowledge of the functions of the body's individual systems and organs. These however do not exist in a vacuum; one is dependent upon the other to allow the body to function normally.)

Nancy K. Brown only uses Aloe Vera (Aloe barbadensis), cultivated in Northern Mexico, where conditions are ideal. The location meets all the criteria, low, yet sufficient water, with fertile and mineral rich soil. Nancy K. Brown Aloe Vera is immediately processed and stabilized upon harvest. It is processed through a sophisticated filtration - mechanical membrane based, chemical free – process. It is cold processed, not heated, and the whole (entire) leaf is used. The undesirable constituents, namely aloin and aloe emodin, are removed via the membrane filtration process.

This methodology of cultivating, handling and processing Aloe Vera ensures Nancy K. Brown that its Aloe Vera products are potent, stable, effective and deliver results. Rich in vitamins, minerals, non-denatured amino acids, active enzymes and among the highest long chain polysaccharide counts in the industry. A standard many health and wellness companies can never hope to match.

Aloe Vera and Glycation

So where does Aloe Vera fit into the story of glycation? Is it, as has been suggested by some, a contributor to glycation? Or is Aloe Vera a promoter of health and a valuable ally in the fight against disease and the adverse conditions and processes of ageing, such as glycation?

Yes, Aloe Vera contains mannose-6-phosphate (mannose); yes Aloe Vera assists with and increases cross-linking in collagen. The questions to ask are: why and how? To merely say Aloe Vera contains M-6-P and cross-linking takes place, thus glycation is caused by Aloe Vera, thus "Aloe vera has a glycation problem" is a distortion of the evidence and demonstrates a complete lack of understanding. It is akin to saying, someone drowned in water, and thus water is bad for you, because water has a drowning problem. So stop drinking or using water.

With regard to mannose-6-phosphate (M-6-P), its role in Aloe Vera, as a constituent, is to function as an anti-inflammatory agent and active growth substance, promoting cell regeneration.[22, 23, 24, 24a]

This is of particular importance in wound healing, which is the body's response to tissue injury, activating a process of which the aim is the "restoration of tissue integrity"[23]. The body's ability to heal wounds is very complicated; putting great demands on all of the body's systems, in a carefully orchestrated, multiphase process. The process can be crudely divided into three main phases: inflammation, granulation tissue formation and remodeling of the extracellular matrix.[24] Aloe Vera, when applied directly to the wound site or ingested, can play a very important and beneficial role as a stimulator and facilitator during the wound

repair process.[24]

In the first phase – inflammation- the components of the extracellular matrix, GAGs and PGs, play an important role. 'They prevent blood coagulation within the vascular space, regulate inflammatory cell function and form the major components of the ground substance on which collagen and elastin fibres are subsequently laid (they form the scaffolding upon which collagen and elastin are deposited). GAGs, particularly hyaluronic acid, also function as regulators of cellular proliferation, migration and differentiation, and growth factor activities. The synthesis and degradation of GAGs' and PGs is thus of paramount importance for proper wound healing.'[24]
When wounds were treated with Aloe Vera "significant qualitative and quantitative changes in the GAG content were observed" [24], this was not the case in untreated wounds. (see notes B and C for explanation of GAGs [A] and PGs [B])

Aloe Vera increases the amount of glycohydrolases (responsible for the removal of the damaged connective tissue matrix in the wound, not unlike the demolition and removal crew at a worksite), during the inflammatory process. Aloe Vera assists in controlling this process of breaking down (removing / recycling) collagen in the connective tissue of wound sites, preventing the uncontrolled destruction of the extra-cellular matrix.[25] This results in an efficient and orderly increase in matrix turnover.[24]

In the second phase – granulation tissue formation – the 'synthesis of the connective tissue matrix'[23] occurs. Collagen, the major component of granulation tissue, is increased in content in wounds treated with Aloe Vera. This is due to Aloe Vera's stimulation of collagen synthesis and its role in increasing the proliferation of collagen synthesizing fibroblasts.[23]

Initially type III collagen, (which establishes the primary wound structure, guides inflammatory cells and fibroblasts into the wound site, provides a matrix to re-establish blood supply and regulates collagen fibre diameter and organization) is most prevalent.
Aloe Vera treated wounds exhibit a greater synthesis of type III collagen than untreated wounds.[23] Type III is rapidly replaced in concentration by type I collagen (which provides the ultimate mechanical integrity of the tissue). [23] When wound healing nears completion they return to their normal ratios.

Following synthesis by fibroblasts, collagen is secreted into the matrix where it is cross-linked to form into fibers.[23] Aloe Vera treated wounds demonstrate a greater degree of cross-linking than untreated wounds. Cross-linking is important as it determines the strength and integrity of the final structure of the healed wound. The cross-linking associated with the stimulatory effect of Aloe Vera is not the same as the cross-linking associated with glycation.

Regular cross-linking of collagen and other proteins is necessary for the proper construction, organization and functioning of tissues and organs. It is the abnormal (nonreversible) cross-linking, associated with glycation and AGEs, which is detrimental. During glycation-initiated cross-linking, the normal repair processes (i.e. replacement cycle of the proteins and turnover of the matrix) is disrupted. This leads to deterioration of the quality of the tissues and organs, degrading their functioning and compromising bodily functions and processes.

The initial proliferation of type III collagen in Aloe Vera treated wounds speeds the healing process and results in a better-organized network of type I collagen. This in turn results in a more stable wound. The increase in Aloe Vera stimulated cross-linking of collagen results in increased wound strength.[28] The result is a faster, more efficient, stronger, better-organized repair of the wound, with minimal or no scaring.

In the third phase - remodeling of the extracellular matrix - the effects of Aloe Vera become evident through its effect on collagen content and ultimate strength of the healed wound.

Wound healing can be compared to the effort required to organize the chaos and repair the damage caused by a bomb blast. Aloe Vera provides the stimulatory activity, which assists in improving the organizational network directing the restoration of order, with minimization of damage. Aloe Vera's other properties assist in lessening the collateral damage, such as bacterial infection and other complications.

As stated above, oxidative stress is an important factor in glycation, as free radicals facilitate the process. It is thus postulated, "that antioxidants may prevent <u>increased</u> crosslinking of collagen in diabetes and ageing."[20] The 2001 study by Bonnafont-Rousselot et al and the 2000 study by Lee et al demonstrated that this is correct. Anti-oxidants (free radical scavengers) can act in one of two manners:

(1) prevent the cellular action of AGEs or

(2) by inhibiting AGE formation, by scavenging reactive carbonyl intermediates.[26]

Aloe Vera provides powerful anti-oxidant action, due to - amongst other properties - its vitamin content, especially vitamins A, E [26, 27], and C. In addition to its innate anti-oxidant properties and constituents, Aloe Vera has the ability to stimulate the body's own anti-oxidant activities. This results in reduced oxidative stress, which has been shown to "play an important role in age related diseases" (Ikeno et al, 1998, 1999).

Aloe Vera also contains amino acids, with particular note lysine, which have "anti-glycating effect."[30] In the 2003 study by Sulochana et al, lysine demonstrated a 76% anti-glycating activity.[30]

Further evidence for anti-glycation properties of Aloe Vera can be found in studies with diabetics, both animal and human. Diabetes mellitus, marked by insulin deficiencies and resultant inability to properly utilize glucose in the blood, has been demonstrated to benefit from Aloe Vera's hypoglycemic effects. Diabetics, due to high levels of unregulated blood glucose, demonstrate more advanced and pronounced forms and stages of glycation. Aloe Vera assists in reducing blood glucose to more normal levels specifically in type I and type II diabetics, not in non-diabetics.[31] This indicates that the activity of Aloe Vera is condition specific.

In the ground breaking 2002 study by Yuji Ikeno et al, the long-term effects of Aloe Vera ingestion were investigated. The researchers found that "Aloe vera ingestion appears to exert some beneficial effects on various age-related diseases without obvious injurious effects…".[32] Aloe vera appeared to "suppress multiple causes of death" and thus "life-long Aloe vera ingestion does not cause any obvious harmful and deleterious side effects, and could also be beneficial for the prevention of age-related pathology."[32] It is safe. The researchers concluded "long-term Aloe vera ingestion lightens the disease burden during the aging process."[32] Although these results were obtained from the use of a mere 1% Aloe vera, the benefits of higher concentrations can be inferred.

The evidence comes to a clear conclusion: Aloe Vera assists the body with its functions, in a preventive and corrective manner. This unique botanical helps the body cope with stresses (such as free radicals), assists with the repair of wounds and injuries, and helps in the fight against disease. Aloe Vera shows particular activity in the fight against the adverse conditions and processes of ageing, such as glycation.

CONCLUSION

From the above information, it can be seen that glycation is a serious problem, part and accelerator of the ageing process. Although ageing is inevitable, the manner and speed of the process can be influenced. Identification of the mechanisms that lead to and accelerate the aging process, offers the ability to improve the quality of life. This is only true if the information is acted upon. It is possible to age gracefully. There is no evidence that Aloe Vera causes glycation or contributes to the ageing process, in fact the scientific research and clinical studies have determined the opposite to be true.

Glycation and its deleterious effects can be, through the identification of the causes, mitigated. Adequate protection from UV radiation, sun or other source; a sensible and balanced diet; avoidance of tobacco; adequate vitamin and anti-oxidant intake; and attention paid to one's general health can help in the fight. Proper skin care can also be of benefit in maintaining the general health and youthful appearance of the skin for as long as possible.

Aloe Vera, properly prepared as described above, used internally and/or topically, can provide great benefit. Its constituents provide direct effect or stimulate the body's natural defenses, including those against glycation and ageing.

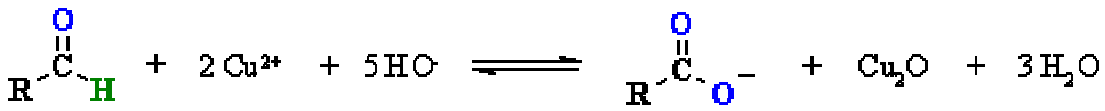
Aloe Vera assists the skin in remaining healthier, more vibrant and more youthful through its hydrating, moisturizing, tissue repair, collagen stimulating, increased matrix turnover stimulating, enhanced bio-availability, immunostimulation, yeast control, anti-bacterial, anti-viral, anti-fungal, anti-inflammatory, anti-oxidant, and yes, anti-glycation activities.

Your skin can look better, longer – really!

Nancy K. Brown is a pioneer in the development of skin, body, hand, foot and nail care products that delivery true results. The only company with a complete skin care line based on real Whole Leaf Cold Processed Aloe Vera. Nancy K. Brown has pioneered the use of Glycolic Acid, Salicylic Acid, effective Environmental Protection products and revolutionized the Skin Care industry with the introduction of concepts such as Hydration, Preventive and Corrective Care, but above all Real Results.
Our motto is 'RESULTS, NOT PROMISES'.

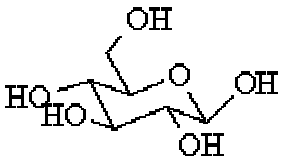
NOTES:

A) Reducing Sugars

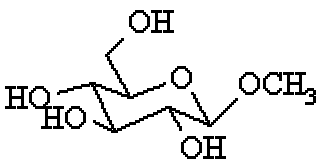


aldehyde carboxylate red precipitate

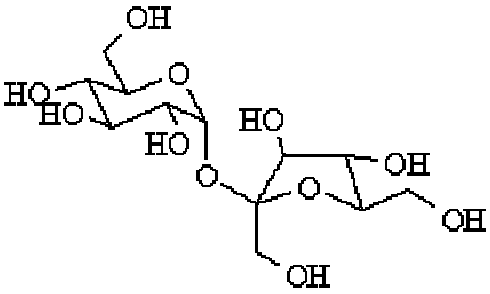
- Sugars that contain aldehyde groups that are oxidised to carboxylic acids are classified as **reducing sugars**.
- Common test reagents are :
  - Benedicts reagent ($CuSO_4$ / citrate)
  - Fehlings reagent ($CuSO_4$ / tartrate)
- They are classified as **reducing sugars** since they **reduce** the Cu^{2+} to Cu^{+} which forms as a red precipitate, copper (I) oxide.
- Remember that aldehydes (and hence aldoses) are readily oxidized.
- In order for oxidation to occur, the cyclic form must first ring-open to give the **reactive aldehyde**.
- So any sugar that contains a **hemi-acetal** will be a reducing sugar.
- But glycosides, which are acetals, are not reducing sugars.



β–D-glucose



methyl β-d-glucopyranoside



sucrose

hemi-acetal => reducing sugar

acetals => non-reducing sugar

- Ketoses can also be reducing sugars because they can isomerise (a tautomerisation) to aldoses via an enediol:

B) PGs – proteoglycans, are heterogenous, non-fibrillar components of the extracellular matrix. The main component of the ground substance. Immediately following an injury, inflammation and the synthesis of ground substance takes place. They are macromolecules made up of a protein core linked covalently to linear heteropolysaccharides, the GAGs.[24]

C) GAGs – glycosaminoglycans, linear heteropolysaccharides, part of the extracellular matrix Regulate cellular proliferation, migration and differentiation. They also direct the activities of growth factor (GF).[24]

PGs and GAGs – form the first bodily responses to wound healing and tissue reconstruction. They prevent blood coagulation within the vascular space, regulate inflammatory cell function and form the major components of the substructure upon which collagen and elastin are deposited.[24]

D) The study, by the Department of Chemistry, University of Scranton found that supplementation with Aloe Vera improves the absorption of both vitamin C (water-soluble) and vitamin E (lipid-soluble). The rate of absorption is slowed and as a result the vitamins last longer in blood plasma, increasing vitamin efficacy and benefit.

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