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AN OVERVIEW OF FUTURE PROSPECT OF *ALOE VERA* GEL AS NANO DRUG CARRIER

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Abstract: *Aloe vera (Linn.)* also known as *Aloe barbadensis* has been used for medicinal purposes in several cultures for millennia: Greece, Egypt, India, Mexico, Japan, and China. The therapeutic claims made for *aloe vera* range over a broad list of conditions, as do the pharmacological activities associated with it. Most of these claims are based on historical use rather than hard evidence. It has been used for centuries in the treatment of sun burns, deep thermal burns and radiation burns, abrasions and other skin irritations. Its use as nanodrug carrier has been reported by several scientists. Increasing interest in this area has been focused on controlled drug delivery using biocompatible polymers as carriers in recent years and aloe gel is an example of such category. Its ease of extraction and processing has made it possible to be used as nano drug carrier. Aloe gel has been reported to be used in successful and controlled delivery of Aspirin and Vitamin C. It has bright future in drug delivery because of its abundance and varieties available throughout the world. The aim of the present work is to evaluate the importance, effectiveness and future prospect of a medicinal aromatic plant *aloe vera* in the field of nano drug delivery.

Key Words: Drug delivery, Controlled drug delivery, Nanotechnology.

1. Introduction: The traditional use of excipients in drug formulations was to act as inert vehicles to provide necessary weight, consistency and volume for the correct administration of the active ingredient, but in modern pharmaceutical dosage forms they often fulfill multi-functional roles such as modifying release, improvement of the stability and bioavailability of the active ingredient, enhancement of patient acceptability and ensure ease of manufacture. New and improved excipients continue to be developed to meet the needs of advanced drug delivery systems .These excipients or drug carriers may be in the form of biopolymers such as polysaccharides, proteins, lipids etc. which may be of plant origin or animal origin (for eg. Alginates, Chitosan, Pullulan ,Aloe gel etc.) or some synthetic biodegradable polymers. In current work the emphasis is given on the structure, properties and uses of *aloe vera* as nano drug carrier in modern and herbal nanotechnology.

Aloe vera (synonym: *Aloe barbadensis* Miller) belongs to the Liliacea family, of which there are about 360 species. *Aloe vera* is a cactus-like plant that grows readily in hot, dry climates and currently, because of demand, is cultivated in large quantities. Cosmetic and some medicinal products are made from the mucilaginous tissue in the centre of the *aloe vera* leaf and called *aloe vera* gel. The peripheral bundle sheath cells of *aloe vera* produce an intensely bitter, yellow latex, commonly termed aloe juice, or sap, or aloes. The name alloeh meaning ‘bitter’ because of bitter liquid found in the leaves. It is also called as ‘lily of desert’ the plant of immortality and medicinal importance with qualities to serve as alternate medicine.

2. Chemistry of *Aloe vera*: The fresh gel mainly consists of water (99.1%) and mesophyll cells (0.9% dry matter), which can be divided into 3 distinct fractions: cell wall, microparticles, and liquid gel [accounting for 16.2%, 0.7%, and 83.1% of dry pulp (w/w), respectively]. The predominant sugar component is mannose as mannose-6-phosphate[1] in all 3 fractions [(20.4% in cell wall, 32.2% in microparticles, and 62.9% in the liquid gel (% of total sugars)], followed by other sugars in varying concentrations depending on the fraction. Overall, the five neutral sugars (i.e., arabinose, xylose, mannose, galactose, glucose) account for 69.2% of the total sugars in the gel[2]**.** Mucopolysaccharides are mainly present as acemannan [a highly acetylated, β-1-4-linked polysaccharide (> 1kDa) made mainly of mannose] with various side chain glycosylation patterns[3]**.** The anthraquinone content should be below 50 ppm and is considered an impurity from the leaf extract of *aloe vera*. Seven other ingredients include various amino acids, enzymes, and vitamins, which have not been quantified. (fig. 1a and 1b)

Aloe vera leaves and the exudate arising from the cells adjacent to the vascular bundles. The bitter yellow exudate contains 1, 8 dihydroxy anthraquinone derivatives and their glycosides[4] .Many investigators have identified partially acetylated mannan (or acemannan) as the primary polysaccharide of the gel, while others found pectic substance as the primary polysaccharide. Other polysaccharides such as arabinan , arabinorhamnogalactan, galactan, galactogalacturan, glucogalactomannan, galactoglucoarabinomannan and glucuronic acid containing polysaccharides have been isolated from the *Aloe vera* inner leaf gel part[5]. A controlled delivery system of glibenclamide using aloe mucilage was studied[6].

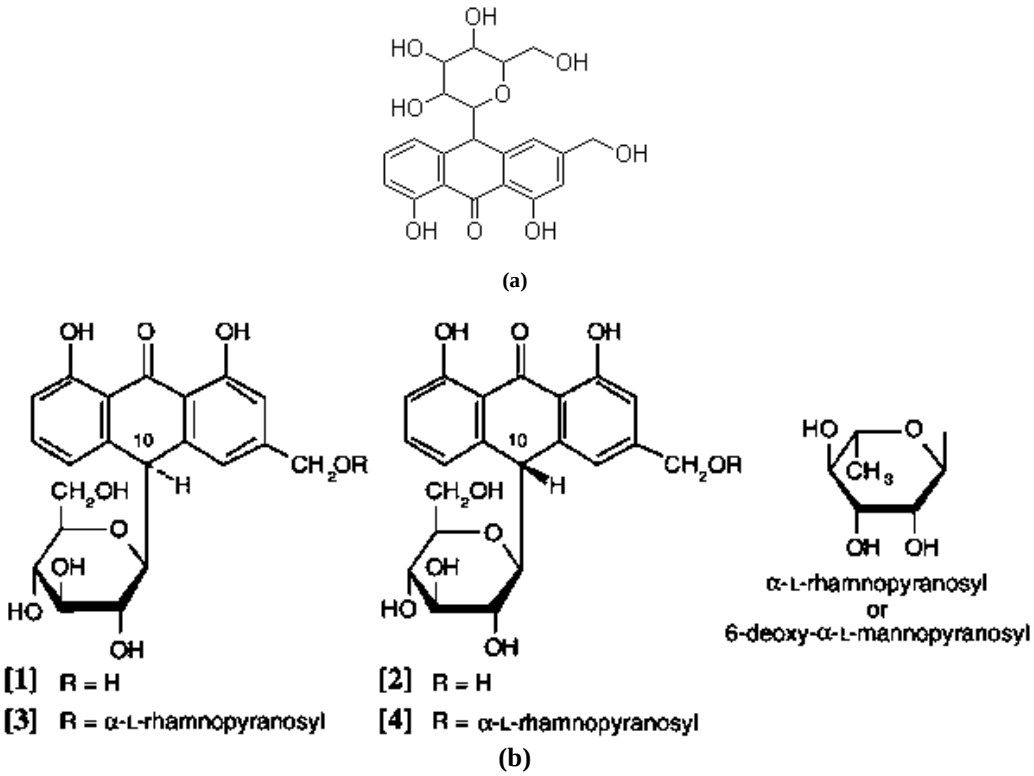

Fig.1 (a) structure of aloin , (b) Chemical structures of some costituents of *aloe vera*

The chemical composition of *aloe vera* varies with species and varieties so the exact composition of *aloe vera* is yet not known. Following **Table 1 and Table 2** describes the major chemical constituents in *aloe vera* and their relationship with the properties of *aloe vera* respectively**.**

Table 1 Constituents of *Aloe vera*[7]

S.No.	**Anthraquinones**	**Inorganic compounds**
1.	Aloin	Calcium
2.	Barbaloin	Sodium
3.	Isobarbaloin	Chlorine
4.	Anthranol	Manganese
5.	Aloetic acid	Zinc
6.	Ester of cinnamic acid	Chromium
7.	Aloe-emodin	Potassium sorbate
8.	Emodin	Copper
9.	Chrysophanic acid	Magnesium
	Saccharides	**Enzymes**
1.	Cellulose	Cyclooxygenase
2.	Glucose	Oxidase
3.	Mannose	Amylase
4.	L-rhamnose	Catalase
5.	Aldopentose	Lipase
	Vitamins	**Essential amino acids**
1.	B1	Lysine
2.	B2	Threonine
3.	B6	Valine
4.	Choline	Leucine
5.	Folic acid	Isoleucine
6.	C	Phenylalanine
7.	α-tocopherol	Methionine
8.	β-carotene	
	Nonessential amino acids	**Miscellaneous**
1.	Histidine	Cholesterol
2.	Arginine	Triglycerides
3.	Hydroxyproline	Steroids
4.	Aspartic acid	β-sitosterol
5.	Glutamic acid	Lignin
6.	Proline	Uric acid
7.	Glycine	Gibberellin
8.	Alanine	Lectin-like substance
9.	Tyrosine	Salicylic acid

Table 2. Chemical composition and properties of *Aloe vera*[8]

Constituents	Number and identification	Properties and activity
Amino acids	Provides 20 of the 22 required amino acids and 7 of the 8 essential ones	Basic building blocks of proteins in the body and muscle tissues
Anthraquinones	Provides Aloe emodin, Aloetic acid, alovin, anthracine	Analgesic, antibacterial
Enzymes	Anthranol, barbaloin, chrysophanic acid, smodin, ethereal oil, ester of cinnamonic acid, isobarbaloin, resistannol	Antifungal and antiviral activity but toxic at high concentrations
Hormones	Auxins and gibberellins	Wound healing and anti-inflammatory
Minerals	Calcium, chromium, copper, iron, manganese, potassium, sodium and zinc	Essential for good health
Salicyclic acid	Aspirin like compounds	Analgesic
Saponins	Glycosides	Cleansing and antiseptic
Steroids	Cholesterol, campesterol, lupeol, sistosterol	Anti-inflammatory agents, lupeol has Antiseptic and analgesic properties
Sugars	Monosaccharides: Glucose and Fructose Polysaccharides: Glucomannans/polymannose	Anti-viral, immune modulating activity of acemannan
Vitamins	A, B, C, E, choline, B12, folic acid	Antioxidant (A, C, E), neutralises free radicals

3. *Aloe vera* as nanodrug carrier : Nanosized particles acquire unusual but beneficial properties which may find industrial applications in biotechnology as well as other fields with equal tendency [9-10]. The specific size of nanoparticles is considered to be of great importance for their application as cell marker in bio-sensing, bio-imaging and targeted drug delivery etc. [11-12]. When used as delivery vehicle, the nano-size range of the particles of therapeutic importance not only makes them suitable for development of systemic, oral, pulmonary, transdermal and other routes of delivery but also helps in increasing bioavailability, protection of bioactivity, stability and eventually in targeted delivery of the drug of interest.

Several plant extracts have been reported to possess unique properties of synthesizing metal based nanoparticles such as Leaf extracts from *Aloe vera*, *Azardirachta indica* have been used in the synthesis of gold, silver, cadmium and bismuth nano-particles. [13-15] .

Gavhane Yogeshkumar *et al* ,(2010) reported the stability enhancement of aloe gel by formulating the polyelectrolyte beads of chitosan and sodium alginate. The study revealed that the formulation of aloe gel into beads significantly improved the compatibility and stability.[16]

Subramanian, K. *et al*, (2010)studied release characteristics of Aspirin and Paracetamol drugs from tablets with *aloe vera* gel powder as a drug carrier. The investigations demonstrated that plant derived natural biopolymers with medicinal values may be successfully employed as a drug carrier for controlled and desirable drug delivery applications with additional health

benefits associated with the herbal extracts used as carriers and excipient by fine tuning the tablet composition and media pH.[17]
Suseem S.R. *et al*, 2013, formulated and evaluated hydrogel with ascorbic acid using *aloe vera* gel powder as a drug carrier. The in vitro release studies showed that the drug was released at a pre-determined rate over a controlled period of time hence they concluded that aloe gel can be used in sustained drug delivery, as materials used in studies were bio available and biocompatible hence they did not impart any toxicity and side-effects.[18]

Owais M *et al* , (2012) reported *aloe vera* induced biomimetic nanosized particles while using 5-FU as model drug. The 5-FU nano- particles synthesized by using *Aloe vera* leaf extract were characterized by UV, FT-IR and fluorescence spectroscopic techniques. [19]

Candokena E *et al* 2014 reported the cytotoxicity of Aloe Emodin on different cancer cells and cocluded that the tumour cells could have an impact for targeting cytotoxic mechanism and Aloe Emodin may be applicable to design novel analogs or derivatives of these natural anticancer agents in future drug research.

4. Therapeutic uses of aloe gel : *Aloe vera* shows numerous properties on the basis of which it can be applied for various applications. Some of such applications are discussed as follows-

1. **Wound healing:** A more recent review concludes that the cumulative evidence supports the use of *Aloe vera* for the healing of first to second degree burns [20]. The wound healing property of *Aloe vera* gel has been attributed to Mannose-6-phosphate [21]. Actually, glucomannan and plant growth harmone gibberellins interacts with growth factor receptors of fibrobroblast and stimulate its activity and proliferation for increases collagen synthesis in topical and oral administration of Aloe according to Hayes [22].

2. **Antitumor Activity:** A number of glycoproteins present in *Aloe vera* gel have been reported to have antitumor and antiulcer effects and to increase proliferation of normal human dermal cells .However, statistically significant clinical studies on the efficacy of *Aloe vera* gel on human health are very limited and often inconclusive [23].

3. **Effects on the Immune System :** In a study on mice that had previously been implanted with murine sarcoma cells, acemannan stimulates the synthesis and release of interleukin-1 (IL-1) and tumor necrosis factor from macrophages in mice, which in turn initiated an immune attack that resulted in necrosis and regression of the cancerous cells . Several low-molecular-weight compounds are also capable of inhibiting the release of reactive oxygen free radicals from activated human neutrophils **[24]**.

4. **Medicinal Uses :** A number of glycoprotein present in *Aloe vera* gel have been reported to have antitumor and antiulcer effects and to increase proliferation of normal human dermal cells **[23].** Gel is useful in ulcerative colitis and pressure ulcers, respectively. Traditionally, *Aloe vera* gel is used both, topically (treatment of wounds, minor burns, and skin irritations) and internally to treat constipation, coughs, ulcers, diabetes, headaches, arthritis, immune-system deficiencies **[25-26]**.

5. **Cosmetic & Skin Protection Application :** Aloin and its gel are used as skin tonic against pimples. *Aloe vera* is also used for soothing the skin, and keeping the skin moist to help avoid flaky scalp and skin in harsh and dry weather. The Aloe sugars are also used in moisturizer preparations [27]. Mixed with selected essential oils, it makes an excellent skin smoothening moisturizer, sun block lotion plus a whole range of beauty products.

6. **Other Applications :**Other than above uses there are numerous applications of *aloe vera* such as it shows laxative effect due to presence of antraquinone. It has also been reported to have Moisturizing and Anti-Aging effects along with antiseptic and antidiabetic effects. Its moisturizing effects have also been studied in treatment of dry skin associated with occupational exposure where *Aloe vera* gel gloves improved the skin integrity, decrease appearance of acne wrinkle and decrease erythema [28]**.** The five phytosterols of *A. vera*, lophenol, 24-methyl-lophenol, 24-ethyl-lophenol, cycloartanol and 24-methy-lenecycloartanol showed anti-diabetic effects in type-2 diabetic mice [29]**.** *Aloe vera* contains polysaccharides which increase the insulin level and show hypoglycemic properties [30].

5. Conclusion: The studies in the present work reveals that *aloe vera*, a natural polymer can be successfully employed as a nano drug carrier which will impart multiple health benefits and which in turn will minimize the side effects of the drugs unlike in the tablets fabricated using synthetic biocompatible polymers as drug carriers. Hence it can be concluded that this plant derived natural polymer may have a great potential to be used as nano drug carrier for controlled and desirable drug delivery applications**.**

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