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THE PHARMACOLOGICAL IMPORTANCE OF *ALOE VERA*- A REVIEW

Ali Esmail Al-Snafi

Department of Pharmacology, College of Medicine, Thi qar University, Nasiriyah, P O Box 42, Iraq.

ABSTRACT

Aloe vera contained anthraquinons and their derivatives, these included barbaloin, aloe-emodin-9- anthrone, isobarbaloin, anthrone-C-glycosides and chromones. The gel or mucilage which obtained from the flesh of the leaf contained an emollient polysaccharide, glucomannan, acemannan, bradykininase salicylic acid, amylase, lipase, and carboxypeptidase. The previous studies showed that *Aloe vera* produced laxative, wound healing, anti-inflammatory, analgesic, antimicrobial, immunomodulatory, antioxidant, cytotoxic, anti ulcerogenic, cardiovascular and endocrine effects.

Keywords: *Aloe vera*, Constituents, Pharmacology.

INTRODUCTION

Herbal medicine is the oldest form of medicine known to mankind. It was the mainstay of many early civilizations and still the most widely practiced form of medicine in the world today. Plants generally produce many secondary metabolites which are bio-synthetically derived from primary metabolites and constitute an important source of many pharmaceutical drugs. *Aloe vera* contained anthraquinons and their derivatives, these included barbaloin, aloe-emodin-9- anthrone, isobarbaloin, anthrone-C-glycosides and chromones. The gel or mucilage which obtained from the flesh of the leaf contained an emollient polysaccharide, glucomannan and acemannan, bradykininase salicylic acid, amylase, lipase, and carboxypeptidase. The previous studies showed that *Aloe vera* produced laxative, wound healing, anti-inflammatory, analgesic, antimicrobial, immunomodulatory, antioxidant, cytotoxic, anti ulcerogenic, cardiovascular and endocrine effects. The present review will highlight the chemical constituents and the pharmacological and therapeutic effects of *Aloe vera*.

Synonyms: *Aloe barbadensis* Mill., *Aloe Chinensis* Bak., *Aloe elongate* Murray, *Aloe indica* Royle, *Aloe officinalis* Forsk., *Aloe perfoliata L., Aloe rubescens DC, Aloe vera L. var. littoralis* König ex Bak., *Aloe vera L. var. chinensis Berger, Aloe vulgaris* Lam [1].

Taxonomic classification
Kingdom: Plantae
Subkingdom: Tracheobionta
Superdivision: Spermatophyta
Division: Magnoliophyta
Class: Liliopsida
Subclass: Liliidae
Order: Liliales
Family: Aloacea
Genus: Aloe L
Species: *Aloe vera* (L.) Burm [1].

Common names
Arabic: Subaar, Subair, Elwa; English: aloe vera, Barbados aloe, Curaçao aloe, true aloe , West Indian aloe; French: aloès vulgaire; German: echte Aloe; Portugese: babosa, babosa-medicinal , erva-babosa ; Spanish: acibar, aloe, sávila ; Swedish: äkta aloe [1].

Distribution
The plant is native to Southern and Eastern Africa, it introduced in Northern Africa, Arabian Peninsula, China, Gibraltar, Mediterranean countries and West Indies. It is cultivated now in many countries [1].

Traditional use
The plant has been used in cosmetic preparations for the treatment of pimples, acne, mouth ulcers, control bleeding, itching of piles, arthritic pains, mild laxative, wash for piles, abscesses and scabies, dysentery and renal colic. The plant also used as emmenagogue, treatment of burns, oedema, pain, swellings and wounds**.** The juice from the leaves was used to increase menstrual flow [1, 2]**.**

Corresponding Author: **Ali Esmail Al-Snafi Email:-** aboahmad61@yahoo.com

Description

It is a stemless or very short-stemmed succulent plant growing to 80-100 cm tall, spreading by offsets and root sprouts. The leaves are lanceolate, thick and fleshy, green to grey-green, with a serrated margin. The flowers are produced on a spike up to 90 cm tall, each flower pendulous, with a yellow tubular corolla 2 to 3 cm long [1].

Part used: The leaf lining (latex, resin or sap) and *Aloe vera* gel were used medicinally.

Physicochemical properties

Total ash not more than 2%, water-soluble extracts not less than 50% and alcohol-insoluble extracts not more than 10% [3-6].

Chemical constituents

***Aloe vera* gel**

The gel or mucilage which obtained from the flesh of the leaf consisted of 99% water with a pH of 4.5 and contained an emollient polysaccharide, glucomannan and acemannan, which were long chain polysaccharides, comprising glucose and mannose [7-10]. The gel also contained bradykininase and salicylic acid [11]. In addition, it contained enzymes, including amylase, lipase, and carboxypeptidase [12-13]. The plant gel also contained minerals such as sodium, potassium, calcium, magnesium, manganese, copper, zinc, chromium and iron, and vitamins, including vitamins A, C, thiamine, riboflavin, niacin, choline, folic acid, and B12. Furthermore, it contained sterols including campesterol, sitosterol and lupeol. Prostaglandin precursors (gamma-linolenic acid), lignins, saponins, and amino acids (arginine, asparagine, glutamic acid, aspartic acid and serine) were also isolated from the gel [14-16].

***Aleo vera* leaf latex**

Anthraquinons and their derivatives were isolated from the latex leaf lining, these included barbaloin, aloe-emodin-9- anthrone, isobarbaloin, anthrone-C-glycosides and chromones [14,17-20].

PHARMACOLOGICAL EFFECTS

Laxative effects

The leaf lining (latex, resin or sap) contained anthraquinone glycosides (aloin, aloe-emodin and barbaloin) which are potent stimulant laxatives. These water soluble glycosides are split by intestinal bacteria into aglycones which have laxative action stronger than senna, cascara or rhubarb root. The anthraquinones found in the latex stimulate chloride and water secretion into the large intestine, inhibit their reabsorption and stimulate peristalsis. The onset of action is 6 –12 hours after a single oral dose. On the other hand, it has severe side effects including diarrhea, nausea, and cramping. For medicinal use, the leaf lining is dried and the residue is used as herbal laxative. The products are taken at bedtime which are poorly absorbed after oral administration. These products excreted in urine, bile, feces and breast milk. The products usually avoided during pregnancy due to the risk of stimulating uterine contractions and during lactation due to the risk of excretion in breast milk [21-24].

Wound healing

Aloe vera gel enhanced wound healing. It reduced wound diameter (induced on both sides of the vertebral column) by 62.5% in mice receiving 100 mg/kg/day orally and 50.80% in animals receiving topically 25% *Aloe vera* [25]. Many studies showed that aloe hasten wound healing cause by burns, frostbite, electrical injuries, caustic chemicals and surgery. It stimulated the activity of macrophages and fibroblasts which increase both collagen and proteoglycan synthesis and promote tissue repair**.** It also enhanced collagen deposition and cross-linking in granulation tissue in wounds and improved scar strength compared with topical antibiotic medication [26-29]. Acemannan also accelerated wound healing and reduce radiation induced skin reactions [30-31].

Anti-inflammatory and Analgesic effects

Aloe vera inhibited the production of prostaglandin E2 by 30% at 1 in 50 dilution (P=0.03), but had no effect on thromboxane B2 production. The release of interleukin-8 by CaCo2 cells declined by 20% (P<0.05) with *Aloe vera* diluted at 1 in 100 [16,32].

Aqueous extract of *Aloe vera* gel showed significant analgesia compared to control. The results were significant (p<0.001) in radiant heat method and also in hot plate method (p<0.05) at the dose of 300 mg/kg. Writhing test showed maximum inhibition (51.17%) at the dose of 300 mg/kg. No adverse effects on renal and hepatic functions were found with *Aloe vera*. Histopathological study of gastrointestinal mucosa showed preservation of normal architecture with *Aloe vera*. The aqueous extract of *Aloe vera* gel has been reported to reduce anti-inflammatory and analgesic effects via inhibition of prostaglandin production from arachidonic acid. It has been utilized for reducing pain during dental treatments, mouth ulcers, sores, blisters, hemorrhoids and for wound healing [33-35].

Antimicrobial effects

Aloe gel exerted antibacterial activity against *Staphylococcus aureus, Streptococcus pyogenes, Serratia marcescens, Klebsiella pneumoniae, Pseudomonas aeruginosa, E. coli, Salmonella typhi* and *Mycobacterium tuberculosis*. Aloe-emodin also inhibited the growth of *Helicobacter pylori* [36-38]**.** The activity of leaf pulp and liquid fraction of *Aloe vera* was evaluated against plant pathogenic fungi, Rhizoctonia *solani, Fusarium oxysporum,* and *Colletotrichum coccodes,* They possessed an inhibitory effect on *F. oxysporum* at 104 µl/l and the liquid fraction reduced the rate of colony growth at a concentration of 105 µl/1 in *R. solani, F. oxysporum, and C. coccodes* [39]**.**

Aloe extract treatment of guinea pig that had been infected with *Trichophyton mentagrophytes* resulted in a 70% growth inhibition compared with untreated animals [40]**.** Acemannan alone and with azidothymidine and

acyclovir blocked the reproduction of Herpes and the AID viruses [41-43].

A significantly faster healing time and a higher number of healed lesions than the placebo was recorded in a randomized, controlled double blind clinical trial of 60 men suffering from an initial episode of Herpes simplex infection, treated with an *Aloe vera* extract (0.5%) in a hydrophilic cream [44].

Immunomodulatory antioxidant and cytotoxic activity

When *Aloe vera* extract (150 mg/ kg and 300 mg/kg) administered to mice for 5 days, it significantly increased the total count of white blood cell and macrophages [45]. Acemannan increased monocyte and macrophage activity and cytotoxicity, stimulated killer T-cells, enhanced macrophage release of interleukin–1 (IL-1), interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α), and interferon gamma (INF-γ)[46-52]. Treatment with *Aloe vera* appeared effective in reducing genotoxicity of the direct-acting mutagen [53].

A. vera exhibited significant inhibition on Ehrlich ascite carcinoma cell (EACC). The order of activity: barbaloin>aloe-emodin>octapeptide>aloesin. A significant concentration-dependent cytotoxicity against acute myeloid leukemia and acute lymphocytes leukemia cancerous cells was recorded. Aloe-emodin was found to be active against two human colon cancer cell lines (DLD-1 and HT2), with IC_{50} values of 8.94 and 10.78 microM. It also exerted activity against human acute myeloid leukemia cells, with significant elevation in the activity of antioxidant enzymes SOD, GST and tGPx [54]. Acemannan has demonstrated activity against feline leukemia virus and solid tumors [10, 55-58]. Treatment of 46 dogs and cats suffering from spontaneous tumors with acemannan, resulted in histopathologic evidence of tumor necrosis in 26 and significant clinical improvement in 12. It appeared that soft tissue sarcomas were more susceptible to the treatment [56].

Anti ulcerogenic effect

Aloe-emodin inhibited growth of *Helicobacter pylori* in a dose-dependent fashion. *Aleo vera* inhibited gastric acid secretion in mice and rats and has protective effects against gastric mucosal damage in rats. Pretreatment with *Aloe vera* extract reduced aspirin-induced gastric mucosal injury by 70% in experimental rats. *Aloe vera* extracts also suppressed the ulcerogenic effects of stress in experimental rats. Intraperitoneal injection of ethanol extract exerted a gastroprotective effect in acute gastric mucosal lesions induced by 0.6 M HCl in rats. A clinical study showed that *Aloe vera* gel might be helpful in treating patients with duodenal ulcers [38, 59-63].

Cardiovascular effects

Aloe vera gel lowered triacylglyceride levels in liver and plasma. Histological examinations of periepididymal fat pad showed that *Aloe vera* gel reduced the average size of adipocytes [64].

Five thousand patients of atheromatous heart disease, presented as angina pectoris, were studied over a period of five years. After adding the (Husk of Isabgol) and *(Aloe vera*) to the diet, a marked reduction in total serum cholesterol, serum triglycerides, increased HDL, decreased fasting and postprandial blood sugar level in diabetic patients were noted. Simultaneously the clinical profile of these patients showed reduction in the frequency of anginal attacks [65].

Endocrine effects

Aloe gel decreased blood sugar in diabetic and normal mice. It also decreased insulin resistance in mice [64, 66-68]. In clinical trials, it appeared that orally administered *Aloe gel* (1-2 tablespoons twice daily) enhanced the hypoglycemic effect of glibenclamide [69-70].

Toxicity and contraindications

The gel stings a bit when it is first applied. It also causes contact dermatitis. Acute toxicity associated with the leaf lining is mostly gastrointestinal including severe cramping, diarrhea, and nausea. Overdoses have also been associated with nephritis, gastrointestinal hemorrhage, dyspnea, palpitations and fluid depletion. Due to side effects, aloe latex has been replaced by other safer laxatives. Long-term ingestion of aloe leaf lining lead to potassium deficiency, muscle weakness and cardiac arrhythmias. Long-term use of anthraquinones is also associated with development of Pseudomelanosis coli. The treatment should be avoided during pregnancy and lactation. 100-150 mg / Kg of *Aloe vera* extract induced abortion in pregnant female rats [71-75].

Dosage

Aloe gel is applied topically three to four times daily for cosmetic or vulnerary purposes Aloe leaf lining comes in a powder, or in aqueous and aqueous-alcoholic extracts in powder or liquid form. Unless otherwise prescribed, the individually correct dosage is the minimal amount to maintain a soft stool (typically 50 –300 milligrams in a single dose) [41, 76].

CONCLUSION

The paper reviewed *Aloe vera* as promising medicinal plant with wide range of pharmacological activities which could be utilized in several medical applications because of its effectiveness and safety.

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