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Anschrift des Verfassers:
Johannes Seidemann
Schubertstraße 1
DDR-1505 Potsdam-Rehbrücke

ALOE DRUG IN HUMAN THERAPY

by

Ralph Holt Cheney Sc.D.

Emeritus Professor of Biology, Brooklyn College;
Brooklyn College of Pharmacy;
and Honorary Research Associate, Brooklyn Botanic Garden.

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History

Centuries of recognition in folklore medicine inform us of the biomedical use of *Aloe* but without sufficient, critical pharmacological evidence to justify its current applications and therapeutic claims for its rapid promotion of the healing process subsequent to skin injury and burns. This 'status quo' makes a reconsideration and testing of its efficiency mandatory especially in view of the fact that the 1962 Amendments gave the United States Food and Drug Administration the authority to assess effectiveness, as well as the safety, of drugs. The agency has relied largely on the advice of non-government experts convened by the National Academy of Sciences. An excellent report on the folklore uses and commercial exploitation of the *Aloe* Leaf Pulp was published in 1961 by Julia F. Morton [1]).

The fresh juice from the leaves and also preparations, such as aloin (barbaloin) its chief constituent drug, derived from the inspissated or dried mass have been utilized for a multiple of unrelated human illnesses [2]), [3]). The principal use *internally* has been as a cathartic; and, *externally* in the treatment of eczematous conditions of the skin and other cutaneous diseases and disturbances such as burns and other surface wounds. A review of the

literature reveals medical reports regarding *Aloe* from ancient records as early as the 4th century B.C. when, under the name of 'mussabbar', it was employed for inflamed, painful parts of the body. Cole and Chen [4]) in an article on *Aloe vera* in Oriental Dermatology; and, Stuart [5]) state historically that the fresh leaf of *Aloe* (or Lu Hui) during the Tang Dynasty (618-905 A.D.) was used externally for sinusitis by local application; and internally for reducing fever in children. A Chinese scholar, Lui Yu-hsi (772-842 A.D.) derived dramatically improved results by applying the fresh leaf on his eczematous skin during his trip to Tibet. During the Sung Dynasty (960-1276 A.D.) *Aloe* was employed for dental diseases and eczema. In the Ming Dynasty (1368-1643 A.D.) *Aloe* was prescribed as a cathartic, antihelminthic and anti-convulsive control in children by internal administration in the form of a galenical preparation. Colonel Tchou [6]) reports that during his childhood in Western China, his burned thumb and index finger was treated with the exuding jelly from a cut leaf of *Aloe vera,* known to the Chinese as 'Jelly Leaks'. The immediate soothing effect and rapid healing within a few days was dramatic. Colonel Tchou also reports his experience 38 years later in Cleveland, Ohio, when he suffered extensive ulceration of the sole of his right foot due to a radium overdose 2½ years previously in China where he had been treated for a cutaneous ailment. His physician friend, Dr. H. N. Cole, treated Col. Tchou with the fresh exudate from *Aloe vera* and it resulted in complete healing rapidly. According to the U.S. Dispensatory [7]) *Aloe* was cultivated on the Island of Socrota at the time of Alexander the Great and it is mentioned in the writings of Dioscorides and Celsus.

Recently, Collins & Collins [8]), Loveman [9]), Rovatti & Brannan [10]) report with enthusiasm the quick and complete healing of skin burns due to ultraviolet, gamma and x-ray injuries. Foster [11]) calls attention to the fact that *Aloe vera* has been popular in the tropics and occasionally in northern temperate zones as a kitchen windowsill plant. It is grown as a houseplant in this fashion in order to have the fresh leaf always available because of its usefulness for cuts and burns encountered in housework. It treats the injured area chemically and forms a quick protective coating as it dries on the skin and it can be washed off readily.

Although the employment of *Aloe* in modern Western Medical Practice has disappeared largely as a cathartic agent, except as an ingredient in the complex known as Tincture of Benzoin (Friar's Balsam), the use of *Aloe* for skin injury has increased currently in the United States and particularly in the State of Florida. Trade Name preparations sold as Alo Ointment, Agic Cream, and Aloe Gel are receiving considerable demand for skin cosmetic purposes, chapped hands, shampoo, sunburn, accident burns and cuts, and even in the hospital treatment for excessive x-ray burns. A new industry,

Aloe Creme Laboratories, Inc., exists in Florida and the products are packaged in attractive plastic jars and bottles.

Botany

Botanically, all *Aloe* species are perennial succulents and confusion exists in the taxonomy, chemistry, and the Trade Names for the raw product plant sources of the *Aloe* on the commercial market. There are approximately 170 species of the genus *Aloe* of the Liliaceae. This genus should not be confused with the so-called 'American Aloe' which is the genus *Agave* of the Amaryllis family. Most of the true *Aloe* species are native to Eastern and Southern Africa. Some species have been introduced into the West Indies, East Indies, Europe and the Americas. *Aloe* drugs from Africa are obtained from Wild plants; whereas, West Indian *Aloe* drugs are harvested from Cultivated plants. The three common commercial Trade Names are I. Socotrina Aloe, originally cultivated on the Island of Socotrina and now obtained principally from East African and Arabian Coastal areas; II. Curaçao Aloe from the West Indies; and, III. Cape Aloe, chiefly from Southern African species. The chief commercial source is *Aloe barbadensis* Miller (synonymous with *Aloe vera* Tourn. ex Linn. and *Aloe vulgaris* Lamarck). It is the major species grown in the Introduced Areas and distributed as Curaçao Aloe; whereas, the principal species gathered in African areas is the *Aloe ferox* Miller and its hybrids and is distributed as Cape Aloe.

Parts used and production

Fresh leaves or the exudate therefrom and the dried paste are employed. It should be *emphasized,* however, that *if Aloe* gel is dried before being incorporated into commercial products, it has been reported to lose its medically efficacious properties. Also, one to two hours is the effective life of an application. A fresh preparation can be applied safely as often as desirable or convenient [8]). Within a few hours the original fresh, light yellow-green color becomes a dark gummy mass which can be washed off with warm water, using no soap or medication [8]).

The *Aloe vera* flowering stalk averages up to 2 feet in height and the thick, translucent, straped-shaped, pale-green leaves (1½ ft.) long are 2 to 3 inches thick and possess awl-shaped soft spines on their margins. Individual leaves are arranged in a fanshaped basal clump showing white-streaked spots when young. A thick epidermis covers the medicinal jellified material. This jelly oozes out so commercially this 'juice' is collected readily from cut leaves by a trough and transported to a 'boiling house' where it is concentrated in copper evaporation pans. It is then poured into gourds or boxes to harden and shipped. The yield increases with the age of the plant

up to four years and then declines but continues to produce for ten years. A four-year old plantation will yield 500 to 1000 pounds of prepared *Aloe* per acre [12]). Off-sets are planted 6 to 12 inches apart in rows 2 feet apart [13]). In 1942 the United States imported 801,300 pounds of *Aloe* valued at $ 238.904. Imports were from the Netherlands West Indies, British West Indies, Arabia, Africa, Venezuela, and a very small quantity from the Dominican Republic. In 1968, in addition to the domestic production in Florida, the U.S. imported some *Aloe* but the quantities, countries, and values are difficult to determine accurately. The U.S. Dept. of Commerce Statistics list *Aloe* imports only as one item in a group category including *Aloe,* Jalap, Maté, Aconite, and Cocculus indicus. This complex of items in 1968 was 505.425 pounds valued at $ 410.480 according to TSUSA (Tariff Schedule U.S. Annotated) No. 4350500 [14]).

Chemistry

The chemistry of *Aloe* exudates has never been determined adequately. The milky material flows from epidermal vessels and possibly only from this source. It is not less than 50 % of a water-soluble extractive containing a mixture of anthraquinones, anthranols, anthrones and their glucosides. By further processing, the Aloin, the chief constituent drug, is obtained. Chopra and Ghosh [15]) reported no aloin in *Aloe vera* var. *officinalis*. Two decades later, however, the twentieth edition in 1957 of Ghosh's Pharmacology, Materia Medica and Therapeutics [16]) offers a suggestion of the action Aloes and Aloin as an emmenagogue. It states that aloin stimulates the uterine muscles and by stimulating the pelvic circulation it causes congestion of the uterus and thereby functions as an emmenagogue and may act as an abortifacient and therefore contra-indicated in pregnancy. No mention is made of the use of *Aloe* or Aloin in relation to burns or any thermal injury. Griffenhagen [17]), editor of the Handbook of Non-Prescription Drugs (1968), does not list Aloin and it is not included in the Modern Drug Encyclopedia & Therapeutic Index for 1965 [18]) nor in the Current Drug Handbook for 1968 [19]). The Merck Index, Ed. 8 (1968), however, lists numerous helpful references to the chemistry of *Aloe* and its derivatives, presenting rather detailed data on *Aloe,* Aloe-Emodin, Aloetic Acid, and Aloin (Barbaloin) [20]). The editors, Paul G. Stechar et al of the Merck Index indicate the generally accepted structural formulas but the organic configurations of Aloe derivatives do not reveal the significant pharmacological potential of these units.

Medical evaluation and experimentation

When one considers the numerous recommendations by Das [2]) for the oral administration of the *fresh* juice for improvement in such a variety of

human conditions as general debility; to correct suppressed menstrual cycles (emmenagogue); to enhance sexual excitement (aphrodisiac); to develop the mammallary glands; and the external application to the forehead to relieve headaches; as well as for burns and skin diseases, one is tempted to wonder whether or not *Aloe* has any true medicinal value or is purely historical folk-fore? Two of these uses, however, for burns and as a laxative, have persisted for centuries. Medical case-histories and some experimental investigations by registered physicians during the last 30 years document the use of Aloe affirmatively for the alleviation and rapid healing of skin injuries.

In 1932, Watt and Breyer-Brandwijk reported [21]) South African tribal uses, particularly by the Zulus, of decoctions from twelve *Aloe* species consumed internally for 'blood scours' in calves, enteritis in fowls, a leaf decoction just prior to parturition to assist the process, tapeworm infection; and, externally rubbing of the green leaf pulp of *A. marlothii* A. Berg. over breasts to hasten weaning of children [21]). In 1935, Collins and Collins [8]) reported in a 31-year old white woman, a case of severe roentgen dermatitis with desquamation over an area 4 by 8 cm of the forehead and extending above the hair line. Within 24 hours after treatment with *fresh Aloe,* the itching and burning had subsided completely! Within 5 weeks with continued treatment, there was complete regeneration of the skin of the forehead and scalp, new hair growth, complete restoration of sensation, and absence of a scar. After 3 months, there was no indication of a relapse and upon exposure to sunburn, the forehead was seen to be pigmenting normally along with other exposed skin surfaces.

In 1937, Lovemen [9]) reported two cases of 40 year old men suffering from severe roentgen ray ulcers on the back of both hands. Treatment with the *fresh Aloe* leaf reduced ulceration areas 50 % within a few weeks and complete healing within a few months. In 1961, Foster [22]) states that Rodney Stockton, a chemical engineer in Florida devised methods for separating the *Aloe* Gel from the leaf and stabilizing it for the manufacture of a Burn Ointment. In 1962, Foster [23]) records the use of *Aloe ferox* gel for eye infection and for hair shampoo in the Phillipines. The Russians also grow and use Aloe gel medicinally.

In 1959, Rovatti and Brennan [10]) reported an experimental study using Albino Rabbits to show the comparative immediate and delayed histopathological changes of the skin in Aloe-treated and non-treated thermal burns. Biopsy specimens were taken from the burned areas at intervals of ½ hr., 1 hr., 2, 6, 24, and 48 hours; and, after 4, 6, 10, 12, 14, 18, 25, 29, and 35 days which was grossly the completion of the pathological process. Comparison was made between Group I Rabbits treated with an Alo-Creme Ointment; Group II treated with the same ointment but containing 5 % cystine;

Group III treated with trinitrophenol ointment; and Group IV treated with petrolatum and gauze. Group I skin remained pliable and soft during the first week and continuous superficial debridement of upper dermis occurred and without gross or microscopic separation of an eschar. The lesions healed in 2 weeks without gross evidence of scarring. Group II showed more of the superficial debridement during the 2nd week but otherwise the results were similar to Group I. Group III Rabbits did not survive 10 days. Group IV Rabbits survived after numerous hemorrhages and small abscesses accompanied by the entire dermis debriding in large masses. The lesions healed with scarring within 1 month. This paper by Rovatti and Brennan [10]) lists 14 bibliographical references and was conducted with careful technique.

In 1964, Goff and Levenstein [24]) using 147 male Mice and based upon 274 determinations found a direct relationship between lapsed time of repair and wound strength, as measured tensiometrically. Of 6 ointments tested the ointment prepared from *Aloe vera* indicated some transitory degree of stimulation of healing. In 1963, Fly and Kiem [25]) state that gel from the macerated central portion or from the complete leaf of *Aloe vera* does not inhibit Staphylococcus aureus nor Escherichia coli. Bacteriostatic evidence was presented in 1964 by Lorenzetti et al [26]) that the fresh juice, if tested immediately, inhibited Staphylococcus aureus 209 but the principle responsible for the inhibitory activity was unstable. They also reported the action of a solution of *Aloe* freeze-dried juice (20 mg./ml. in distilled water) diffusion technique for bacteriostatic activity against 8 microorganisms. They found significant inhibition of growth on plates innoculated with Staphylococcus aureus 209, Streptococcus pyrogenes, Corynebacterium xerose, and Salmonella paratyphi. They concluded that the freeze-dried juice, when previously heated to 80 degrees for 15 minutes, could be kept refrigerated for some time and would inhibit these 4 microorganisms. The freeze-dried whole leaf, *minus the juice,* i.e. the leaf mesophyll and epidermis, does not have bacteriostatic properties.

Final comments

Persistent and continuous agreement through the centuries by ancient and modern medical men can not be ignored wisely. This spectacular biomedical evidence of the value of this botanic source of a therapeutic material for cuts and burns demands new investigations to discover the detailed chemical constituents of *Aloe* and to determine their individual pharmacologic action responsible for their apparent efficacy. Currently the known organic structures involved [20]) do not supply us with any obvious reason to anticipate their significance in the healing process.

In February 1969, Gyanchandani, Yamamoto, and Nigram [27]) described a new procedure for the identification of Aloes and other botanic source

laxatives by thin-layer chromatography. In addition there is a lack of critical information regarding the effect of *Aloe* constituents on the growth of micro-organisms. Particularly important is the unknown or non-convincing reports on the effect of *Aloe* on Pseudomonas aeruginosa (syn. Bacillus pyrocyaneus). As noted by Beckman [28]) Pseudomonas aeruginosa causes 70 % of all septicemia in burn victims. Although the topical application by mass attack of multi-antibiotics inhibits many causative organisms of septicemia, the suppurative Pseudomonas aeruginosa is still the 'killer'.

It is to be hoped that the research programs of the pharmaceutical laboratories and hospital clinical teams will give the *Aloe* drug the attention it deserves in our age when x-ray and other thermal injuries and skin diseases are major problems in medical practice.

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MACHTVOLLE AFRIKANISCHE PFLANZEN ERZEUGEN VERGESSENHEIT

Stete Suche nach neuen Arzneimitteln

Jungen Knaben in Westafrika, die aus Versehen allzu früh Einblick in geheime Riten der Mannbarmachung bekamen, wird ein Vergessenheits-Trunk aus einer bestimmten Pflanze gegeben. Die Wirkung: sie vergessen für dauernd alles, was sie nicht sehen sollten. Ebenso benützt ein Stamm in Ostafrika, die Tongas, den Saft einer Pflanze, um kleinen Säuglingen, die von der Mutterbrust entwöhnt werden sollen, die Erfahrung des Säugens vergessen zu machen.

Vergessenheits-Pflanzen in Afrika und Südamerika

Diese Erfahrungen und solche ähnlicher Art wurden auf einem dreitägigen Symposium an der Harvard-Universität in Cambridge mitgeteilt, das dem Thema 'Pflanzen in der Entwicklung der modernen Medizin' gewidmet war. Dr. John M. Watt, der Professor für Physiology an der Universität von Queensland in Australien, berichtete auf dieser Tagung über die Verwendung von Vergessenheits-Drogen bei den afrikanischen Eingeborenen. Die erwähnte, von den Tongas benützte Droge kommt von einer afrikanischen Pflanze, Annona senegalensis.

Auf der gleichen Tagung erstattete Dr. S. Henry Wassen, der Direktor des Ethnographischen Museums in Gotenburg, Schweden, ein Referat über südamerikanische Pflanzen, welche die Fähigkeit besitzen, Vergessenheit hervorzurufen. Er erwähnte dabei den Bericht eines Reisenden, der darüber unterrichtet worden war, daß Gefangene mit dem Extrakt dieser Pflanze behandelt wurden. Dieser Trunk sollte sie ihr Heimatland und ihre Treue zu dessen Herrschern vergessen machen. Ein anderes Kraut, so berichtete Dr. Wassen, wird beim Genuß alkoholischer Getränke im Mund gehalten, und das hilft mit Sicherheit dazu, die Erzeugung von Trunkenheit zu verhindern.