ANALYSIS OF CACTUS GRANDIFLORA.

BY

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THESIS

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This plant, ordinarily termed "Night Blooming Cereus," is also known by the botanical name, Cereus Grandiflorus (Miller) of the Cactaceae, but Cactus Grandiflora (Linæi) seems to be given the preference. In medicine, according to Maisch's Organic Materia Medica the fresh flowering, weak, fleshy, five or six angled, spined, branches, are used in the form of a tincture made entirely with alcohol. By Lloyd Brothers, manufacturing pharmacists of Cincinnati, Ohio, these stems are obtained just after flowering time, from a firm of florists at Hamilton, Ohio and made immediately into the tincture. Parke, Davis and Co., manufacturing pharmacists of Detroit, Michigan, however on the other hand claim to import their fluid extract directly from Mexico, where it is prepared. The habitat of all the Cactaceae is well known to be the West Indian Islands and it is reasonable to suppose that constituents of plants grown there may
differ from those grown in northern United States. However, no
difference in physiological action seems to be noticed in the use of
the drug as prepared by these two firms, although the dose
recommended by the two firms differs, as is usually the case
with fluid extracts and tinctures and in about the usual pro-
portion.

A few years ago when the supply of Cactus Grandi-
flora, was insufficient to meet the demand, substitutes were
sought in allied plants. It does not appear that any of these
substitutes have proved in any way superior to that first em-
ployed. It is now easy to obtain the latter and, perhaps merely
because it is better known, physicians seem decidedly to
prefer it. The other species being, therefore, little in demand,
have disappeared from the market. Cereus Bonplandi was
one of the foremost of these substitutes, but clinical experiements
with it do not differ materially in results from those performed
with Cereus Grandiflora.
An allied plant to the above is Cactus flagelliformis, of which, the stem and branches are weak, thin, several feet long, thin angled, warty, spiry, and bear red flowers and small wooly hairs. The acridulous juice is reported to be anthelmintic. It contains, according to L. A. Buchner (1836) acid calcium malate, potassium acetate, albumen, mucilage, etc.

Long ago, says the National Dispensatory, Cactus (Grandiflora) juice was known to be extremely acid, producing vesicles and pustules, and when taken internally causing vomiting, colic and bloody stools. In substance and in tincture, it was used as a vermifuge (Richter Arzneimittelkunde ii 290). In 1868 it was stated that the tincture of the plant had been used advantageously by Rubini, in functional palpitation of the heart. (Med. Record iii 299). in 1878 Dr. W. S. Davis confirmed the earlier statement (Phila. Med. Times X 20) and in 1883 Dr. Byrd reported, that it palliated the abnormal action and the pain, in rheumatic disorders of the heart, and was even beneficial.
to the rheumatism itself (ibid. 611). The general agreement
of opinion, in recent years, regarding it, is as follows: Cactus,
like Digitalis, slows the heart, while increasing its energy and
raising the arterial tension, but unlike the latter, it displays
no cumulative action, nor does it tend, like Digitalis, to produce
extreme contraction of the heart, resulting in sudden arrest of
its action; usually employed as a tincture or fluid extract, in
doses of 6m 3-6 (mu - x) 2 or 3 times daily.

Cactus has been deemed a very valuable
remedy and indeed almost specific in certain diseases of the
heart. The following abstract from Seudders' Eclectic Materia
Medica and Therapeutics (83) indicates its specific value; viz.

In uneasy sensations in the region of the heart; as of difficult
or irregular movement; oppression in the praecordia; irreg-
ularity of the pulse as to time; a sense of unsteadiness and
irregular contraction when the finger is placed on an artery.
Therapeutic action:- The influence of Cactus seems to be wholly
exerted on the sympathetic nervous system, and especially upon
and through the cardiac plexus. It does not seem to depress
or increase innervation (neither sedative or stimulant), but
rather to influence a regular performance of function. Its con-
tinued use improves the nutrition of the heart, thus permanently
strengthening the organ. It has a second influence upon the
circulation and nutrition of the brain, and may be employed
with advantage in some diseases of this organ. We can see
very readily how this may be. The cardiac nerves are derived
from the upper part of the sympathetic, and judging from the
anatomy of the part, the first cervical ganglion, being the
principal nerve mass in the cervical region, must furnish in-
nervation through the cardiac nerves, as it certainly controls the
circulation and nutrition of the brain.

Caolin is a specific in heart disease, in that it
gives strength and regularity to the innervation of the organ. Its
influence is permanent, in that it influences the waste and
nutrition of the heart, increasing its strength. It exists no influence upon the inflammatory process, and hence is not a remedy for inflammatory disease.

Feelings of weight and pressure at the praecordia, difficult breathing, fear of impending danger, etc. are at once removed. Such irregularity of action, whether violent, feeble or irregular, as is dependent upon the innervation is readily controlled. Thus, in the majority of cases of functional heart disease, it gives prompt relief, and if continued will effect a cure. In those cases in which there is another lesion acting as a cause, as in some gastric, enteric, or uterine lesion, this must receive attention and be removed to make the cure radical.

In structural heart disease, the first use of remedies is to relieve the distressing sensations in the region of the heart, and the unnatural fear of danger which attends them. As these spring from disordered innervation, in the majority of cases Pulsus gives prompt relief. As we have seen
above, its continuance favors normal waste and nutrition, as well as regular action. Hence, its continued use is followed by the removal of adventitious tissue, and an increase in the strength of its contractile fibre. Thus it proves curative in many cases of structural heart disease. But it will not relieve or cure cases of valvular deficiency, dilatation of the openings of the heart or fatty degeneration. In its influence upon the nervous system, it more nearly resembles Pulsatilla, giving relief in that condition known as nervousness. Further, it gives regularity of cerebral function and improves the nutrition of the nervous centres.

Maisch ascribes emetic, cathartic and vermifuge properties to Cactus but clinical experiment does not bear this out. Parke Davis and Co. publish a brochure upon the pharmacological value of both Cereus Grandiflorus and Cereus Bonslau-dii embracing clinical reports from private and hospital practice.

In view of the above, which seems to prove that
Cactus is really a valuable medicinal agent; I undertook an investigation into its chemical, therapeutical and pathological natures as well as pharmacological as is given above. Work of this kind has been done as said above in the case of Cereus Flagelliformis and also by the German chemist, L. Lewin, upon several representatives of the Cactaceae. A general review of the work done by him and others is given in Band 11, 1894, "Berichte der Deutschen Botanischen Gesellschaft." The whole of his work on Cereus Grandiflorus, seems to be embodied in the following translated abstract: "The juice of Cereus Grandiflorus causes, by long contact with the skin, unbearable itching, erosions and blisters. If one burns the juice in a room, it causes, after breathing the fumes, sneezing, running at the nose, inflammation of the mouth, and spitting of mucus and blood. If one takes it into the stomach, then, owing to the local irritation, vomiting takes place, and after its passage into the intestines dysen-
teric stools are induced." In an allied plant, Anhalonium lewinii, he found a crystalline, salt-forming alkaloid of the formula \( \text{C}_2\text{H}_3\text{N}_2\text{O}_3 \), of which 0.2-0.4 grams was fatal to animals. This alkaloid he named "Anhalonin." Further toxicological, chemical, and crystallographical properties of this alkaloid may be found in his record in the Archiv für experim. Pathologie und Pharmakologie" Bd. 34. 1894.

My experimental results do not seem to at all corroborate the above statements with regard to the expressed juice of the plant. When applied by me to the skin of the lower forearm for 1½ hours, no iritant effects could be noticed. I also heated some of the juice in a porcelain dish until nothing but the ash remained, holding my nose in the fumes all the time and with very little inconvenience. The only way these results may be reconciled, is by the fact that plants grown in different countries may have widely differing properties, although the two plants be identical.
The stems I used in most of my experiments grew in the green house of Frank's the florist in Champaign, Illinois. These stems appeared to be identical with those used by Lloyd Brothers and Co. manufacturing pharmacists of Cincinnati, Ohio, having obtained a sample from the growers of the plant they use. Their stems are grown at Hamilton, Ohio and cut just after flowering in August when they are fleshiest. Those I used were cut in January and February, so that according to the experience of manufacturers of preparations of the drug, they are not quite so valuable.

The action of Caelius upon a medium sized dog I found to be similar to the foregoing description of its action upon the human being. The heart was greatly stimulated when large doses were given. After three doses of five drops each of Parke, Davis and Co's Fluid Extract the heart beat was stimulated from ninety (normal) to one hundred and twenty beats per minute. The pulsations were also more regular and stronger.
Smaller doses (two drops) induced increased regularity and strength of action without so much increasing the number of beats per minute. The same action was produced upon the dog by my preparation (a tincture with alcohol 90 and sliced stems IV ⅓ macerated three days) except that it required a larger dose to produce the same amount of stimulation. Both preparations produced considerable diuresis. This effect has been noticed upon the human and indeed the remedy is strongly recommended by physicians as a diuretic. The above seems to indicate that domestic grown stems have all the medicinal values of the plant and I believe that the majority of firms preparing it use the domestic-grown stems.

Proximate Analysis.

The percentage of moisture in the sliced stems, air dried and powdered in a mortar. = 8.97\% Moisture.

The mineral matter or Ash, estimated by igniting at
low red heat, above powder in a porcelain crucible = 18.45% Ash.

A qualitative analysis of the ash determined the presence of Carbonate of Calcium, Sodium and Potassium.

Per Gunnung Method 69% = Total nitrogen.

The systematic analysis of the stems of the Cactus I carried on by the successive application in a definite order of solvents and reagents as follows. (According to a scheme of plant analysis, Lyons Pharmaceutical Assaying Pages 38 - 41 inclusive.)

A. - Treated 5 gms finely divided, air dried stems with Benzol, wholly distilling below 86°C. by hot percolation.

Benzol extract = 7.6%

Residue (a) - Dried at 100°C and treated 12 hrs. by hot percolation with alcohol (cf. gr. 546)

Alcoholic Extract = 10.1%

Residue (b) - Dried at 100°C weighed and treated with a known measure of cold water.
Macerated with frequent agitation eight or ten hrs. Filtered through paper. 

Water Extract = 12.75% 

Residue (c) - Washed with alcohol, dried at 100°C, and weighed, treated with 100 cc. water and 5 cc. Conc. H2SO4 and heated till a drop gave no color with Iodine solution.

Analysis of solution in Benzol. 
Evaporated to dryness and weighed residue. Treated with water, again evaporated to dryness at 100°C heated to 110°C and weighed again.

Volatilized (Camphor, Camphor Oil etc.) = .42 %

Residue (a) - Treated with a moderate quantity of warm water, and when cold, filtered. 

Aqueous Solution. - Divided in two por's A. B. 
A - Evaporated to dryness and weighed.

Total Extract = .38 % Ash = .06 %
6. Analysis of Alcoholic Extract

- Soluble Ash = 4.8%
- Total Ash = 4.3%
- Reddish-brown precipitate
- Found in plant as Potassium and Calcium Malates

Reddish-brown precipitate with Lead and Sulfate

- Analysis of Solution in Cold Water
- Total Extract = 14.8%

- Treated portions with Mercury Biny's, Picric Acid, Jointing in 1:3 sol., etc.
Above solution being divided into aliquot portions and tested (a) by solution of iodine gave no blue color (absence of starch)
(b) by ammonium oxalate a precipitate, white, (presence of Calcium)
(c) by dilute HCl no gelatinous ppt (absence of pectin or pectic acid)
filtered (c) and treated with four times its volume of
alcohol, no further precipitate (absence of arabinob Dulcis)
The following table shows the percentage extraction
of solvents and of other constituents.

Benzene extract, 7.6 %
Probably consists of wax, resin, chlorophyll, camphors.

Alcoholic extract, 44.6
Probably consists of resin, coloring matter, albumen, Potas. malate,

Water extract, 14.8
Contains gum, pectin, tannins, calcium malate, albumen,

Ash, consisting of carbonates of Potassium and Sodium, 18.41

Moisture, 8.97

Remainder consists probably of cellulose, lignin & Coloring matter.
Experiments upon the juice and extracts.

The stems were sliced transversely into thin discs and placed in an ordinary screw-pressure-press without any strainer except the perforated tin sides and bottom of the press. The use of a cloth, surrounding the sliced stems, through which the juice might be pressed was found to be very unsatisfactory, as the flow of juice was very slow and great strength was required to work the press. 250 c.c. of a light greenish, slimy, mucilaginous, tenacious juice was obtained from 500 grams of the stems.

This is the juice that was used in the experiments as mentioned on page 9 of this thesis, to determine its action upon the skin. As there stated it has very little, if any action upon the skin, although I believe that this juice contains the medicinal principle, whatever it may be.

As there is evidently a great deal of inert matter, consisting of gummy and resinous materials, in the expressed
juice, this was separated by use of alcohol in the proportion of 150 c.c. of the expressed juice to 500 c.c. of alcohol. This precipitate had all the appearances and acted in all respects like a mixture of gums of indefinite composition being whitish, tough, brittle when dry, soluble in water, insoluble in alcohol or ether.

The filtrate was heated to 75-80°C. in a retort, on a water-bath and the alcohol distilled off. When the thermometer rose to above 80°C. the distillation was stopped, the remaining liquid poured out and water added, by which a greenish colored precipitate was separated (probably chlorophyll and a very small amount of resinsious matter. The filtrate was now darker and had lost the green color (chlorophyll). On testing was found to be neutral in reaction. This was shaken up five times with 100 c.c. of ether each time and the ethereal solutions being collected and most of the ether distilled off by means of a water bath, the concentrated ethereal solution was allowed to evaporate spontaneously. The residue (extracted) was yellowish-brown in color, and consisted of oily globules having
a strong vinegar-like smell and neutral in reaction; amount, about one fourth of a cubic centimeter. This probably consisted of camphor, resins and oily matter.

The dark yellow solution remaining after this extraction was made slightly alkaline with ammonia, shaken out and the ether- and ether-extract treated as above was finally brought to dryness in a desiccator. Residue consisted of about one tenth of a gram of white, small, almost indistinguishable, ill-formed crystals. This residue was treated with absolute alcohol and mixed well with it; then filtrate was tested for alkaloids with Myers Reagent (Potassic-Mercuric Iodide), with Iodo-Potassium Iodide solution and with alcoholic Picric Acid solution without any results pointing to the presence of an alkaloid. Another sample of this alcoholic solution was brought to dryness leaving no residue so that nothing was dissolved from the extract by the alcohol. The insoluble white residue was dissolved in water and then precipitated by lead acetate solution. The precipitate, soluble in
nitric acid when boiled with water melts to a transparent mass, it is decomposed by $H_2S$. Evidently the white substance extracted here is the ammonium salt of an acid. These same tests with others which were used are explained on Page 20, where more of the acid was extracted and further tests made.

The aqueous solution remaining from the preceding treatment was shaken with chloroform several times and after separation the chloroform was evaporated by blowing air over its surface. Globules of yellowish, oily, resinous-smelling matter were thus obtained. This was probably resinous camphoraceous compounds.

The solution remaining from above was made distinctly acid with $HCl$ and shaken up with ether as above, the ether distilled off and solution brought to dryness. Residue colorless, and amorphous with a heavy aromatic smell. This also was probably resinous camphoraceous matter.

The remaining solution was then evaporated to
Dryness on a water bath. The residue was a brown amorphous mass, having a salty taste. Weight 1.45 grams. A definite weight of this residue was burned to an ash. Amount of ash represented 48% of the residue so that it residue probably consisted of a brownish coloring matter and according to the qualitative analysis of the ash, Carbonates of Potassium, Sodium and Calcium.

To determine the identity of the acid contained in the plant a tincture was made, taking three liters of alcohol to five pounds of drug and the alcohol distilled from this. An aliquot part of this solution was then precipitated with lead acetate solution and the precipitate well washed, decomposed by H₂S, filtered and brought to crystallization in a desiccator. The acid was, however, too impure and would not crystallize so that it was treated with Ba(OH)₂ solution, filtered and the Barium then precipitated out by a very dilute solution of H₂SO₄ and filtrate crystallized in long tufted needles in a desiccator. This acid gave all the reactions of malic viz, reduction of dichrom
ate of Potash solution in the cold, ammonia salt insoluble in alcohol, solubility of lead salt in ammonia etc.

There is no indication of a principal of glucosidal nature in the plant, as a tincture whose green coloring matter (chlorophyll) has been precipitated by addition of lead subacetate and subsequent dilution with water, gives no rotating power in the polariscope, either before or after warming with dilute acid.

Some of the greenish matter of the plant is undoubtedly extracted in the preparation of the fluid extract as a fluid extract which I made containing twenty per cent of water was similar in color to that of a fluid extract of a brand much used by physicians (P.D. and C.) A determination of the alcohol in their fluid extract gave eighty per cent. The fluid extracts of the drug are darker in color and without the green tinge of the tinctures.

From the results of my work, I must conclude that there is no principal of alkalioidal character in the plant.
All my results and tests seem to point to a series of complex resinous bodies, in which, I believe, the medicinal virtues of the plant lie and to which its peculiar physiological action may be attributed.