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A STUDY OF SYMPHYTUM OFFICINALE

COMFREY ROOT

By

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I wish to acknowledge with thanks the help given
me by Professor W. G. Richtmann in Course 110, in work-
ing the botanical references of this thesis.

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SYMPHYTUM OFFICINALE

Comfrey Root

("Comfrey was first used as a medicinal agent in Europe and the plant has been naturalized in this country!")
King, J. & Newton, R. S. (1852) Electric Dispens. U.S.A.
1 ed., p. 396.

(1) ("In Sarracenus's version of Dioscorides published in 1596, descriptions are given of two species of Symphytum; Chap. IX (Liber II) is headed "De symphto petraeo" and Chap. X "De Symphyto Altero". The "roots" and their "vertues" are described in the following terms:--"Radices demittunter foris nigrae, intus candidae glutinosae, quorum etiam est usus. Tritae et potae sanguinem excreantilius ruptisque proficiunt et recentia vulnera impositae glutinant, curnum quoque frusta quibiscum conpinguntur cogunt ita ut cralescant. Caeterum inflammationibus praesertimque sedis, cum Senecionis foliis utiliter illinunter.")

Bock, in his work , "De stirjuim" (Kyhei's edition, 1552), quotes and expands this sentence from Dioscorides, and describes the then recognized methods of application of the plant, internally and externally. Fuchs also (1542) quotes the same extract, and also the views of Galen and Pliny, which are practically in the phraseology of Dioscorides.

In W. Turner's "Herball" (1568) the following occurs: "of comfrey, Symphytum. The rootes are good if they be broken and dronken for them that spitte blood, and are bursten. The same, layd to, are good to glewe together freshe wounds. They are also good to be layd to inflamation and specially of the fundament, with the leaves of ground-sell". This account is also merely a condensed translation of Dioscorides.

Dodoens in his "Cruydtboeck" translated by Lyte (1578), expands Turner's statement, adding that when "mengled with sugar, syrapes, or honny...are good to be layde upon all hoate tumours". Quite similar statements as to the value of comfrey rhizome are made in Bulleyn's "Herbal" (1562) and in the "Adversaria" of Pena and Labeluis (1570) the "Stirpuim Historia" of the latter author (1576) and in the epitome of Camerarius (1586). J. Bauhin ("Historia", 1651) expresses his concurrence in the views of the sixteenth century herbalists as to the curative value of decoctions of comfrey in all cases of wounds, blood spitting, or even broken limbs.

Gerard's "Herball" (1597) repeats, but at somewhat greater length, the same account. He asserts the efficacy of comfrey also in healing up "ulcers of the lungs" and "ulcers of the kidneies, though they have been of long continuance." Parkinson ("Theatrum Botanicum" 1640) gives the

same general description of the "vertues" of comfrey, but adds: "The rootes of Comfrey, taken fresh, beaten small, spread upon leather, and laid upon any place troubled with the gout, doe presently give ease of the paines; and applied in the same manner, giveth ease to pained joynts, and profiteth very much for running and moist ulcers, gangrene, mortifications, and the like."

In the "Compleat Herbal" of Tournefort (1719) a long account is given of the "vertues" of Comfrey and of its general characters. The author says: "This plant contains a glutinous phlegm in which there is some sulphur but very little sal amoroneac; for upon a chymical analysis the Comfrey yields many acid liquors, much earth, very little sulphur, and no concreted volatile salt, but a small quantity of a urinous spirit and a very moderate quantity of fixed salts; so that its powers seem principally to depend upon its slimy mucelage, which the fire destroys." Tournefort closes his account with the following interesting sentence: "We find among the observations of Hieronymus Rensuerus that a Charlatan cured a certain person of a malignant ulcer, pronounced to be a cancer by the surgeon, and left by them as incurable, by applying twice a day the root of Comfrey bruised, having first peeled off the external blackish barb or rind; but the cancer was not of above eight or ten weeks' standing."

By the end of the eighteenth century comfrey seems to have declined in popularity among physicians; thus Woodville ("Medical Botany," 1794) writes: "A supposed vulnerary efficacy for which this plant was formerly in great repute, and to which it seems to owe its name" (comfrey-confirma), "will now be considered as nothing in its recommendation". He adds: "The mucilaginous matter is the only medicinal principle, and may be used as an emollient and demulcent."

From the experiments recently made by Dr. C. J. Macalister with extracts of the rhizome of *Symphytum* it would seem that conclusions such as those just quoted are somewhat hasty and scarcely just either to the old herbalists who have written on the "vertues" of the plant, or, indeed, to the plant itself.

Symphytum officinale L., is described as possessing a massive vertical "rootstock", passing insensibly into the thick, flesh root which divides into large branches (Somerby, Vol. VII., p. 114). From an examination of the dry material sold as the rhizome of this plant it would appear that both root-stock and roots are used indiscriminately; indeed, the samples I examined seemed to consist mainly of root segments. The general anatomy of the order is dealt with briefly in Soldereder's "Sytemater Anatomy of the Dicotyledons," pp. 554-561 and 1,001-2 and also in greater

detail by H. Jodin "Recherche anatomiques sus les Borranginee (Ann. Sc. Lat. Sec., 8, I. xvii., 1903, pp. 362-346). Jodin does not seem to have examined *S. officinalo* anatomically, and his account of the structure of *S. tuberasum* is in itself sufficiently indefinite. A brief reference to the anatomy of *Symphytum officinalo* is also made by Schlepegrell ("Anat. d. Tubifloren," Bot. Centralbl. 1892, p. 230), who states that the vascular bundles are separated by un lignified tissue. As a matter of fact, the rhizomic structure, save for the great development of succulent parenchyma between the xylema and the feeble development of phleme, appears quite normal for rhizomes with large parenchymatous reserve regions. When sections are treated with mercuric nitrate a white amorphous precipitate is thrown down plentifully in the parenchyma, both of the medullary rays and of the cortex, and this substance, I am informed by my colleague, Dr. A. W. Titherly, is identical with the substance extracted by him from the rhizome, and described by him, in hi paper published in this Journal, as Allantoin.

Allantoin is regarded by plant physcologists as a derivative (probably an oxidation product) of nuclein, and has as yet only rarely been identified in plants. In addition to the literature referred to by Dr. Titherly, Richardson and Crampton (Bes. Chem. Geo., XIX, 1886) have found it in wheat previous to germination; and Thomas has

shown ("Verhandl. Ges. Naturf, Hamburg, 1901) that the substance described by Peckhall as "Cordianin" in species of Cordia is probably identical with allantoin. Czapek ("Brochemie der Pflangen," II., p. 199) regards it as a reserve proteid and add "Analytisch Verhält sich das Allantoin dem Asparagin Ähnlich."

Further investigation is likely to prove the presence of allantoin in many other plants, and in all probability it plays some important part in the constructive metabolism taking place in growing parts, both of the seedling and of the adult. I hope to publish at an early date further observations on the occurrence of Allantoin in such situations as determined microchemically."

The earliest mention of this root appeared in a book, "Historia Plants" by Otto Brunfels in 1530. H. Tragus published his, "De Stirpium" (1552) in which he gives synonyms, descriptions, references, and illustrations of the plant. Carl Linne in his species Plantorum (1753) gives generic and specific names of the plant.

J. Plisson (1829) isolated from the root and small quantity of Asparagan. King and R. S. Newton's authors of the electric dispensatory (1852) gives history, properties,

(1) Pharm. Journ., 88, p. 91.

and official preparations. F. G. Hayne (1853) gives pre-linnian names with illustration of plant. A. Stille and J. March (1829) editors of the National Dispensatory Outlines, synonyms, origin, description, constituents, medical action, and uses. Kohler in "Medizomal Pflenzen" etc. (1898) gives description, name, history, part uses, preparations, constituents, and full sized illustration and coloration of the plant. A. B. Lyons (1900) gives the meaning, generic name, common English, French, and German names, part used with Pharmacautical names and properties of Comfrey.

Since the discovery of the Alkaloid Allantoin from the rhizome of Comfrey, articles have been written on the value of Comfrey for boils. Brunier has published an article in the American Journal of Pharmacy (1919) called "Comfrey Extract for Boils," in which he gives a method for their treatment with Comfrey root.

PHARMACOPOEIA HISTORY OF SYMPHYTUM OFFICINALE

The Danish Pharmacopoeia 1st edition (1772) was the first Pharmacopoeia to contain *Symphytum officinale*. It appeared next in the Swedish Pharmacopoeia (1775) and was official in the first four editions. It was official in six editions of the Spanish Pharmacopoeia from 1794 to 1884. *Symphytum* was official in five editions of the Austrian Pharmacopoeia from 1815 to 1855. It became official in the French Pharmacopoeia (1818) and appeared in five editions up to 1908. Two editions of the Netherland Pharmacopoeia contained the drug 1851 and 1871. It was official in the first two editions of the Romanian Pharmacopoeia 1862 and 1893. The root was official in the third edition of the Portugal Pharmacopoeia (1872) and the first edition of the Siberian Pharmacopoeia (1820). *S. officinale* has never been official in the United States Pharmacopoeia.

METHODS FOR EXTRACTING ALLANTOIN

(1) A preliminary examination of the dried rhizome can be made by digesting with excess of hot water for fifteen minutes and filtering the jelly like resulting mucilage under pressure. The aqueous solution strongly reduced Fehlings solution but gave no starch reaction. A green coloration was produced with Ferric Chloride and gave intense yellow color with sodium hydroxide. The remainder of the solution was treated with an equal volume of absolute alcohol in order to throw out the sugars, dextrans and gummy substances. The precipitate after washing with 50% alcohol gave no coloration with Sodium Hydroxide or Ferric Chloride and did not reduce Fehling solution. It consisted of dextrine like carbohydrates which were not further investigated. The aqueous alcoholic filtrate was concentrated at 40°C to a thick syrup, amounting to about .3 grams from 15 grams of the dried rhizome. After standing for twenty-four hours small needle like crystals formed which were isolated from the syrup with methyl alcohol and draining on a porous plate. The needles were found to be sparingly soluble in cold water. These needles were identified as Allantoin and it was evident that though the separation was very imperfect, the compound or compounds responsible for the color test remained in the syrupy portion.

(2) The dried rhizome was placed in a Socklet and extracted continuously with ethyl alcohol containing 5% water for eighteen hours. In this way practically the whole of the Allantoin was extracted in the form of a solution from which it could readily be isolated using this solvent the dextrans, which proved very troublesome on account of their colloidal properties in aqueous extraction, were not taken out. Three first portions of this solvent were used and after each extraction the brown alcoholic solution was removed. The extractive was then concentrated and allowed to stand in the cold for almost twelve hours, crusts were deposited on the walls of the flask chiefly consisting of Allantoin and sugar. The remaining alcohol was decanted and the flask carefully rinsed with a small quantity of pure alcohol. The alcoholic solution and washing were evaporated at a temperature from 50° to 60°C. and yielded a dark brown syrup containing resins and tannins. The residue was then drained free from alcohol and treated with a very small quantity of cold water, a suspension of sparingly soluble allantoin, together with some insoluble resinous material, was obtained, which was finally filtered. The flask was again washed with cold water and transferred to the filter. The filtrate was evaporated at 50° to 60°C. and a thick brown syrup remained consisting chiefly of sugar which yielded a phenylazozone. The allantoin now remained partly

on the walls of the flask and filter. The portion that remained on the filter was transferred to the flask. Then about 20 cc. of water was poured into the flask and boiled until the crystals were dissolved. The hot solution was then treated with blood charcoal and filtered. The clear filtrate on standing several hours deposited allantoin as clusters of needles and a further crop was obtained by concentrating the mother liquor. The crystals which were finally purified by recrystallization from hot water were perfectly colorless and transparent. They melted at 227°C. with decomposition and gas evolution, and with previous darkening in color.

(1) Pharm. Jour. 88, p. 92.

(2) Pharm. Jour. 88, p. 93.

SYNONYMY(1)

1. Symphytum confolida Major.
 2. Symphytum guidam Inulam rufticam qui dam alum Gallicum vocant.
 3. Confolida Major.
 4. Symphytum Magnum.
 5. Symphytum. Tur. Lon. Majus.
 6. Symphytum Alterum.:
 7. Symphytum Alum.
 8. Confolida Vulgo.
 9. Symphytum Majus flore purpureo.
 10. Confolida major flore albo and purpureo.
 11. Symphytum majus flore purpureo: flore rubio: flore pallido.
- (2)₁. - Symphytum foli s ovatis - lanceolatis decurrentibus.

(1) Bauhin, C. (1671) Pinax, p. 259.

(2) Linne, C. (1753) Species Plantarum 1 ed., p. 136.

ACTION, MEDICAL USES, AND DO SAGE

(1) ("This plant is demulcent and slightly astringent. The mucilaginous agents exert an influence on mucous tissue, of many pulmonary and other infections in which these tissues have been chiefly implicated. The mucilaginous agents are always beneficial in scrofulous and anemic habits. Comfrey root is very useful in diarrhoea, dysentery, bronchial irritation, cough, hemoptysis, other pulmonary infections, leucorrhoea, and femal debility; these being mucous infections. It is also of some value in passive hemorrhages from the bowels, kidneys, or womb.

Externally, the fresh root, bruised forms an excellent application to bruises, risptures, fresh wounds, sore breasts, ulcers and white swelling.

For internal use the root may be boiled in water, wine, or made into syrup, and taken in doses from 1 to 4 fluid ounces of the preparation 2 or 3 times a day. A tincture of the root has been recommended in from 1 to 10 drops doses.")

(1) Kings Am. Dispens., 18 ed., p. 1870.

EXPERIMENTAL

A percolator was set up for continuous extraction and then packed with four pounds of milled comfrey root.

Three preliminary extractions were carried out on the root, each running for eighteen hours respectively. The results from these three extractions are as follows:

First: petroleum ether - 16.806
Gms. of evaporated extract.

Second: ether - 16.308 Gms of
evaporated extract.

Third: Chloroform - 11.702 Gms. of
evaporated extract.

Three different extractions with ethyl alcohol followed. They were run eighteen, twelve and twelve hours respectively. The extractive from all three extractions were poured into one large beaker and allowed to concentrate. Small needle like crystals formed in the syrupy extract, which were isolated and purified by shaking the extract with methyl alcohol decanting off the alcohol and allowing it to evaporate. The crystals were then drained on a porous plate. They melted at 227°C . with a decomposition and gas evolution and previous darkening in color suggested allantoin.

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