CHEMICAL STUDY OF SENECIO AUREUS.*

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The official *senecio* is deserving of investigation if it is at all worthy of being used as a drug. In spite of the facts that *Senecio aureus* is a common plant in the United States, that its use in medicine dates back to days before the first settlers, and that it is an important article of the formulary, apparently no one has ever taken pains to examine it thoroughly from a scientific standpoint. Of the exceedingly numerous species of this genus, several others have received considerable attention, the results of which might tend to show some possible value in medicine, but the properties of *S. aureus* have been entirely unknown. If it is to remain an official article, certainly something should be learned of its composition and physiological action. We have undertaken a study with this in mind, of which the present paper may be considered a preliminary report, and hope to continue it until much more of the chemistry and pharmacology is known.

The genus *Senecio*, as is well known, is the most extensive one in the vegetable kingdom, including as it does upward of one thousand species. These are found in almost all regions on the earth and at various altitudes, although each is individually restricted in range. At least seventy-two species are native in the United States and twenty-seven of these are found in the State of Washington.

S. aureus is indigenous to North America, inhabiting the region from Newfoundland to Florida and west to Ontario, Missouri and Texas. It is commonly known in various localities as golden senecio, ragwort, groundsel, squaw weed, false valerian, grundy swallow, female regulator and life root. The last of these names is recognized by the National Formulary.

The plant was named by Linné in 1753, but for years previously was a favorite with the Indians, who used it as a vulnerary. The white people who first settled in this country learned of its reputation and soon adopted the drug, later applying it also as an emmenagogue. The preparation most often employed was a five per cent infusion or decoction in a dose of two ounces. In 1886 Small introduced the dried herb into medical practice and it eventually became popular with the eclectic and homeopath, On account of the great demand, it was admitted to the National Formulary IV, together with a fluidextract made with diluted alcohol.

There have been a great variety of applications in medicine, some of them apparently little related to the original recommendations. Thus, besides the older employment as healer and as emmenagogue, the drug is now described as stimulant, diuretic, pectoral, antirheumatic, internal hemostatic, etc. It would be interesting to determine, if possible, just how these applications were deduced, considering the absence of published data. It is also interesting to note that a few of the other species have reputations as being valuable for the same purposes, notably *vulgaris, jacobœa, præcox, canicidia, albicaulis, grayanus* and *cervariæfolius*. Some of them are also employed as purgatives, emetics, hypnotics and antiseptics in epilepsy and in fevers. The chief and most common use of all of them, however, is in the treatment of amenorrhea.

In spite of such diverse reputation, there is little evidence in the literature of value for any of these species. There are occasional references to one of them in

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medical journals, but these are merely expressions of opinion and give no controlled methods (see 1, 3, 5, 6, 7, 12, 13, 15, 17, 24). An experimental study of *S. jacobœa* was made by Bunch (16) in 1901, showing that injection of an alcoholic extract in dogs caused rise in blood pressure by constriction of the peripheral vessels, but that lowering of pressure and slowing of the heart followed several injections of larger doses. Watery extracts caused circulatory depression only. The action of the excited uterus of the guinea pig by several drugs was investigated by Pilcher (21) in 1916, who found that *S. aureus* gave very little effect.

Poisoning of animals by species of senecio has resulted in a number of inquiries. Debierre (4), in 1889, presented details of the physiological effects of *canicidia*, which is a Mexican species and, as its name indicates, is used to kill dogs. The potent principle, which caused excitability and convulsions, was most abundant in the root. Cushny (20) found experimentally that extracts of *latifolius* and *vulgaris* caused symptoms similar to those of poisoning which had been encountered, but that *jacobœa* and *sylvaticus* were non-toxic, in spite of suspicion which had been entertained against them. Wilncott and Robertson (22) have described the effects in accidental ingestion of *ilicofolius* and *burchelli* as consisting of gastro-enteritis with ascites, and found cirrhosis of the liver at post-mortem. Cushny and Watt (23) made similar findings.

It can be concluded from the foregoing that several of the senecios contain potent principles but that there is no uniformity. As far as can be learned, no one has investigated the toxicity or pharmacology of *aureus*.

CHEMISTRY OF THE GENUS.

S. cănicidia was reported to contain (2) a poisonous organic acid, senecic acid.

S. kăniferi contains an unsaturated acid (8), C_4H_7COOH, which was named seneciocic acid, but nothing is recorded as to its physiological action.

S. vulgaris was examined by Grandval and Lajoux (9), who isolated two alkaloids, senecionine and senecine, the properties of which were described. Lutz (11) found that undergound portions of *jacobœa, erucœfolius, paludosus* and *cineraria* also gave reactions for these two alkaloids. *Jacobœa* was reported by Altan (18) to contain a glucoside and an unsaturated acid.

From *S. latifolius* Watt (19) extracted two alkaloids, senecifoline and senecifolidine. The analyses and properties of these would lead one to suspect that Grandval and Lajoux may have obtained impure samples of the same compounds.

Muller (25) isolated from *S. fuchsii* an alkaloid, *fuchsisenecionine*, from *S. sylvaticus* a different one, silvasenecine, and from *S. vulgaris* a base whose gold compound was prepared.

OFFICIAL DESCRIPTION.

In the N. F. IV the drug was defined as "the dried, overground portions—gathered when flowering," and was required to yield not more than ten per cent of ash. In the last edition this was changed to read: "the dried plant of *Senecio aureus*," and no standard for ash is included. There may have been good reasons for such alteration, but we have been unable to find any published data which would call for it. The questions which would naturally be elicited are obvious. Which parts of the plant, if any, are potent? Can a definite requirement of maximum

ash be set? Has the activity any relation to time of gathering? Ultimately we hope to answer them.

EXPERIMENTAL.

The material employed in this preliminary work was obtained from a local wholesale house in the form of a very fine powder. It was entirely within the official requirements in every respect, but we have no knowledge of place or time of gathering.

Moisture and Ash.—Samples of the material were dried to constant weight at 110° C. and the loss determined. This varied from 10.66 to 10.92 and averaged 10.76 per cent. They were then ignited and heated according to the U. S. P. method, and the amount of ash was found to be 11.30 to 11.85, with an average of 11.62 per cent. Samples of two other commercial products were found to have 8.33 and 8.76 per cent, respectively. Evidently there is considerable variation in methods of collection or in properties of drug from different localities.

Extraction.—Representative samples were submitted to successive extraction with solvents in the order named. The first two products were brought to constant weight in a desiccator and all of them were finally dried at 110° C. The average results follow in per cent of drug.

	Volatile.	Total.
Petroleum ether	0.56	3.11
Ether	0.45	2.17
Alcohol	..	6.85
Water	..	19.42

All of the extracts were yellow-green to green except that by water which was a black, tar-like mass. The product of alcohol contained crystals, which were found to reduce Fehling's solution and to give the characteristic osazone of glucose.

The Volatile Oil.—When the powdered drug was moistened with water and distilled with steam, there was obtained a milky distillate with a thin film of oil on the surface. This was completely extracted with ether, which was separated, dried with calcium chloride and filtered. The solvent was mostly removed by distillation and the remainder in a vacuum desiccator. From 1000 Gm. of drug there was obtained 2 Gm., or 0.2 per cent of a mobile, yellow oil, which rapidly became more viscid and darker on standing. The characteristic odor gradually became very penetrating and pungent. The taste was sharp and burning; the refractive index at 25° C. was 1.4511. The oil and the aqueous residue both gave a characteristic reaction with aniline acetate for furfural and also for alkaloids by the usual precipitating reagents.

Upon standing the oil deposited yellow, rhombic crystals which melted at 118° C. and burned with the characteristic blue and odorous flame of sulphur. Estimated according to the method in plants as given in the *A. O. A. C.*, the total oil was found to contain 1.22 per cent of this element. It is interesting to note that comparatively few volatile oils contain compounds of sulphur, and they are mostly Liliaceæ or Cruciferæ. As far as is known, no other members of the Compositæ has been found to furnish sulphurous oils.

The Alkaloids.—The drug was exhausted by alcohol, which was filtered, and the alcohol was largely removed by distillation. The residue was extracted repeatedly with two per cent hydrochloric acid, producing a red-brown solution which

gave copious precipitates with Wagner's or Mayer's reagent, and with phosphotungstic acid, phosphomolybdic acid or picric acid. Tannic acid, Dragendorff's reagent, or Marme's reagent gave no reaction. The acid liquid was extracted successively with several immiscible solvents and, after making ammoniacal, again in the same order. The results are given in the following table.

TABLE I.

Acid solution.	Color.	Wagner's.	Mayer's.	Phosphotungstic.	$PtCl_4$.	Picric.
Petroleum ether	Light green	+	None	+	None	None
Benzene	Brown	−	−	−	−	−
Ether	Yellow-green	+	−	+	−	−
Carbon tetrachloride	Yellow	+	−	+	−	−
Carbon disulphide	Colorless	−	−	−	−	−
Chloroform	Yellow	+	+	+	−	−
Amyl alcohol	Red	+	−	+	−	−
Alkaline solution.						
Petroleum ether	Colorless	+	−	−	−	−
Benzene	Colorless	+	−	−	−	−
Ether	Yellow	+	+	+	−	−
Cl_4	Yellow	−	−	−	−	−
CS_2	Yellow	−	−	−	−	−
$CHCl_3$	Yellow	+	+	+	−	+
Amyl alcohol	Yellow	−	−	−	−	−

The ether extract from ammoniacal solution deposited needle-shaped crystals, which were soluble in ether, chloroform or alcohol, but insoluble in water or petroleum ether. After purification, they were found to melt at 112–113° C. and to give no tests for alkaloids. The chloroform extract gave a much larger quantity of crystals which were similar in appearance and melted at the same temperature. Solutions of them in diluted acid gave no positive tests with any of the reagents.

The results indicate that several alkaloids are contained in senecio, some of them so weakly basic that they can be extracted from acid solution. Ether and chloroform are seen to be the best solvents.

Volatile Alkaloids.—The residual marc, left after separation of the volatile oil, was made alkaline with sodium carbonate and distilled with steam. The distillate was milky and had a film of oil on the surface. It gave positive reactions with Wagner's reagent and with phosphotungstic acid. Attempts to collect the precipitate in the latter case by centrifuging and filtration were unsuccessful because it was too finely divided. Extractions with ether gave a small amount of yellow oil which gave precipitates with the alkaloidal reagents. Evidently part or all of the bases present in the drug are volatile with steam.

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THE PREPARATION OF DILUTED HYDRIODIC ACID AND SYRUP OF HYDRIODIC ACID.*

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INTRODUCTION.

The purpose of this paper is to present some practical formulas for the preparation of Diluted Hydriodic Acid and Syrup of Hydriodic Acid by the retail pharmacist. In order that the problem may be viewed in the proper perspective, it will be well to begin with a brief summary of earlier work in this field which has a bearing on the present discussion.

HISTORICAL REVIEW.

Discovery of Iodine and Hydriodic Acid.—Following the discovery of the element, iodine, by the French pharmacist, Courtois, in 1811, hydriodic acid was first recognized by Clement and Desormes (1) in 1813. In the following year, Gay-Lussac (2) prepared hydrogen iodide by passing a mixture of hydrogen and iodine through a red hot tube.

Introduction of Iodine and Hydriodic Acid into Medicine.—Shortly after the discovery of iodine, Coindet (3) suspected that this element was the active constituent of the ashes of sponges, which had long been used empirically in the treatment of goiter and scrofula, and after proving this to his own satisfaction he introduced iodine into medicine. Due to its irritant action, iodine frequently caused severe gastric disturbances, and to overcome this undesirable effect, Dr. Andrew Buchanan (4) of Edinburgh, in 1837, introduced the use of hydriodic acid, which he prepared by the action of tartaric acid upon potassium iodide.

Official Recognition of Preparations of Hydriodic Acid.—Diluted Hydriodic Acid was introduced into the U. S. P. of 1860, was omitted in 1870 and 1880, but was again included in the 8th, 9th and 10th revisions. The method of prepara-

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