

SUMMARY AND CONCLUSIONS.

1. The color of the container in no way affects the character and quantity of the precipitate formation in fluidextract of senna.
2. Observations upon precipitation in fluidextract of senna, to be of value, should be continued over a period of not less than three to four months.
3. Filtering the fluidextract does not seem to affect the rate of precipitation.
4. Precipitation in fluidextract of senna is evidently not due to enzyme activity, as shown by,
 - (a) Heat-treating the drug.
 - (b) The effects of most of the chemical reagents.
5. Fluidextracts of senna with decreasing percentages of alcohol in the menstrua tend to show comparable decreases in p_H , over a certain range.
6. Of the chemical compounds tried, borax was the only one which materially reduced the amount of the precipitate which forms in fluidextract of senna.
7. Fluidextract of senna seemed to show reducing properties.

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CHRYSOPSIS GRAMINIFOLIA, NUTT.—A PRELIMINARY STUDY.*,^{1,2}

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The genus *Chrysopsis* of the *Compositæ* consists of biennial or perennial caulescent herbs, usually conspicuously pubescent. The leaves are alternate; blades very narrow or sometimes broad, entire and sessile or somewhat toothed and petioled near the base of the stem. The heads are showy, radiate or rarely discoid, typically in corymbs. The involucre are many flowered with bracts narrow, several series; the inner ones successively longer. The receptacle is pitted. Ray-flowers are several, pistillate and the disk-flowers mostly perfect. Corollas are yellow. Stigmas with linear or subulate appendages; achenes flattened. The pappus is double with the outer series of small scales or bristles; the inner of numerous rough hair-like bristles (1).

Chrysopsis graminifolia, Nutt. has silvery-silky foliage with long closely pressed hairs. The stems are 3-9 dm. tall, corymbosely branched. The leaves are various, the basal with narrowly linear blades 1-4 dm. long, many times longer than the upper. The stem-leaves do not clothe the stem, with linear-lanceolate, linear or linear-subulate blades, the upper erect. The involucre are cylindric, 10-12 mm. high, 5 mm. thick. The bracts are linear-subulate, glabrate or glandular-pubescent on the back. The ray-flowers have narrow ligules, 8-12 mm. long (1). The herb flowers from July to October and is found growing profusely in dry sandy soil from New Jersey and Delaware to Kentucky and southward to Florida. It has been known variously as "Golden Aster," "Blue-grass" and "Fever-grass" and has been stated to be of medicinal value especially as a poultice for sprains (2).

A review of literature revealed that no studies have been made on this plant, and because of its reputed medicinal value and since it grows so profusely in the Carolinas it was decided to make a study of it to ascertain, if possible, any therapeutically active substances.

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¹ An abstract from a thesis to be submitted in partial fulfilment of the requirements for the degree of Master of Science in Pharmaceutical Chemistry.

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The material used in this investigation was collected in the vicinity of Wiggins in Colleton County, South Carolina. Three collections of the entire herb were made: (1) in the Fall of 1933 just after frost, (2) in July 1934 and (3) in August 1934.

EXPERIMENTAL PART.

A. MOISTURE AND ASH DETERMINATION.

The moisture content of the various lots of the entire herb was determined by the Xylene method (3) and was found to be as follows: Lot No. 1, 9.8%; Lot No. 2, 10.6% and Lot No. 3, 10.8%.

The ash determinations were carried out in the usual way with the following results calculated on the dry basis:

TABLE I.

Lot No. 1, Per Cent.		Total Ash. Lot No. 2, Per Cent.		Lot No. 3, Per Cent.	
A.	B.	A.	B.	A.	B.
6.96	6.59	8.15	8.33	6.26	6.51
Acid-Insoluble Ash.					
3.85	3.56	4.65	4.63	0.78	0.67

B. EXTRACTION WITH SELECTIVE SOLVENTS.

A portion of each lot of the herb was subjected to continuous extraction in a Palkin-Watkins' apparatus (4) until completely exhausted successively by petroleum ether, absolute ether, absolute alcohol and hot water. In the case of the petroleum-ether and ether extracts the excess solvent was evaporated to a small volume and the remainder was allowed to evaporate spontaneously; the alcohol and water extracts were concentrated to a small volume under a vacuum and the remainder of the solvent allowed to evaporate spontaneously. Since previous tests showed the absence of volatile materials the final extracts were dried to constant weight at 105° C. The results of these extractions on the dry basis are shown in the following table.

TABLE II.

Extract Appearance of Extract. Lot No.	Petroleum Ether. Yellow Green.	Absolute Ether. Green.	Absolute Alcohol. Green.	Hot Water. Black Brown.
1	1.55%	1.36%	1.11%	7.29%
2	1.57%	0.69% ¹	1.38%	9.03% ²
3	3.50%	2.29% ³	1.47%	20.87%

¹ Irritating acetic-like odor.

² Sweet licorice-like odor.

³ Irritating odor.

C. PRELIMINARY TESTS.

- (1) The usual elemental tests indicated the *presence of Nitrogen and Phosphorus*.
- (2) Aqueous extracts of the entire herb of all lots were subjected to the following tests:
 - (a) Reaction to indicators was neutral.
 - (b) Ferric chloride solution gave a blue-green precipitate with all lots indicating, at least, *tannins*.
 - (c) Lead acetate solution produced a precipitate with a colorless filtrate which gave a slight precipitate with basic lead acetate solution indicating a number of substances including *tannins, saponins, acids, etc.*

(d) Fehling's and Benedict's solutions showed signs of reduction; upon acid hydrolysis showed increased reduction.

Purified residues from the Stas-Otto process (5) gave positive tests with (a) an alcoholic solution of alpha-naphthol (20%) and concentrated sulfuric acid (blue ring and colored solution on mixing) and (b) an alcoholic solution of thymol (20%) (red color) (c) showed reduction with Fehling's and Benedict's solution before and after acid hydrolysis. These reactions indicate the presence of carbohydrates, glucosides or disaccharides.

(e) Purified extracts from the Stas-Otto process, as well as the aqueous extracts, when tested with alkaloidal reagents, showed the absence of these substances.

(f) The usual tests for cyanogenetic substances with picrate paper showed them to be absent.

(3) Bourquelot's method (6) whereby glucosides hydrolyzable by enzymes can be detected in the presence of carbohydrates such as sucrose, which is hydrolyzed by saccharase, indicated that these substances were absent.

(4) Since saponins are indicated and these are glucosidal in character it was thought that these might be responsible for certain positive tests obtained for glucosides. Kraft's procedure (7) which admits the separation of saponin-like substances from the glucosides was employed. Tests after the separation indicated their absence.

Saponins.—Saponins were isolated by extracting the herb with hot 95% alcohol for two hours under a reflux on a water-bath. On concentrating and cooling the hot filtrate a flocculent precipitate settled out, was filtered off and more saponin obtained by the addition of ether to the alcoholic solution. The precipitate was dissolved in water and purified by the Magnesia method (6). After purification and redissolving in alcohol the saponin was precipitated by fractional precipitation with ether and the amount obtained gravimetrically yielding 0.37% on the dry basis. The purified material gave a positive Sagel Test (8).

Tannins.—Tannins were examined further according to the scheme of Dafert and Fleischer (9) and these tests including that of Stiasny (10) indicated the presence of *catechol* tannins with small amounts of *pyrogallol* tannins. Since the two major groups of tannins were shown to be present these were extracted by the method of Chapman (11) and were determined (a) by the Cinchonine Sulfate Method of Hooper (12) which is stated to estimate the amount of pyrogallol tannins in the presence of others. This determination yielded 0.60% of pyrogallol tannins and (b) the Hide Powder Method of Shröder (6) which gives an estimation of the total tannins present. This content was found to be 3.95%. These results show a probable catechol tannin content of 3.35%. Other extracts which have been obtained and will be studied further also indicated the presence of a *bitter principle*.

SUMMARY.

A preliminary examination of *Chrysopsis graminifolia* is reported which included:

(1) Moisture content varying from 9.8–10.8% for three lots of the entire herb collected at various seasons of the year.

(2) Total ash varying from 6.26% to 8.33%; acid-insoluble ash 0.67 to 4.65%.

(3) Extracts with selective solvents using the Palkin-Watkins' Extractor are determined.

(4) Preliminary tests show the presence of nitrogen, phosphorus, saponins and reducing substances, tannins and bitter principle.

(5) Quantitative determinations show (a) saponins 0.36% and (b) catechol tannins 3.35% and pyrogallol tannins 0.60%.

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THE SYNTHESIS OF UREIDES OF CERTAIN MONOBASIC ACIDS AND KETONES.*

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It is well known that certain ureides prepared from dibasic acids possess marked hypnotic action. In view of this fact it seemed of interest to prepare ureides from brominated aliphatic monobasic acids and ketones with a view to studying their physiological action.

The compounds prepared were: α -bromo-*n*-caproyl ureide, α -bromo-iso-caproyl ureide, methyl- β - β -dimethyl-2-urea α - α -dibromo ethyl ketone and β - β -dimethyl-2-urea- α - α -dibromo ethyl-iso-propyl ketone.

EXPERIMENTAL.

α -Bromo-Caproyl Ureide $C_7H_{13}O_2N_2Br$.—Place a mixture of 56 Gm. of *n*-caproic acid and 3 Gm. of red phosphorus in a 500-cc. round-bottomed flask having a ground glass neck into which is fitted an upright condenser. To the mixture add 71 Gm. of bromine drop by drop and reflux over a water-bath until the contents assume a light yellow color. The brominated acid is separated from the mixture by distillation at reduced pressure. A total of 74 Gm. were obtained. The acid was light yellow in color, possessed a faint but persistent odor, insoluble in water, soluble in alcohol, ether and chloroform; boiling point $131^\circ C.$ at 9 mm.; $d_{23} 0.9404$; $n_D^{20} 1.423$; $[\alpha]_D^{25} -47.46^\circ$ in benzene.

To prepare the acyl chloride derivative an excess (10 Gm.) of thionyl chloride is added to the acid (20 Gm.) in a manner similar to that used in the bromination. Remove the sulfur dioxide by heating on the water-bath and separate the prepared acyl chloride derivative by distillation at reduced pressure. The pure compound (21 Gm.) possessed a boiling point of $98^\circ C.$ at 30-mm. pressure.

The ureide is finally prepared by mixing the brominated acyl chloride (19 Gm.) with urea (18 Gm.) and slightly warmed on a water-bath. The mixture at first liquefies, after which it becomes a solid mass. The mass is neutralized by washing with several portions of aqueous sodium carbonate solution after which it is washed with distilled water.

After several recrystallizations from a hot 50 per cent solution of alcohol the ureide melted at $175^\circ C.$ It consisted of colorless crystals having a slight but persistent taste, insoluble in water and fixed oils but soluble in 95 per cent alcohol, ether and chloroform.

A nitrogen determination showed the compound to contain 11.07 per cent N as compared to 11.45 per cent calculated on the basis of the formula $C_7H_{13}O_2N_2Br$.

α -Bromo-iso-Caproyl Ureide $C_7H_{13}O_2N_2Br$.—The method used in preparing the iso compound was essentially the same as that outlined for the normal compound. Starting with 60 Gm.

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