Potentilla Anserina in Essential Dysmenorrhea

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During some collaborative studies of the Viburnums, interest was aroused in *Potentilla anserina* as an agent of possible use in the treatment of essential dysmenorrhea. To insure against errors in identity, it was decided to secure a supply of the crude drug, and to manufacture an extract from it for use in the investigations herein reported. Great difficulty was experienced in securing authentic *Potentilla anserina*. A number of samples were submitted by several crude drug houses, and these were turned over to Dr. Heber W. Youngken, pharmacognosist of the Massachusetts College of Pharmacy, for identification. Dr. Youngken found that each of the first samples submitted was spurious. Most of them were *Potentilla argentea*, and Dr. Youngken suggested a possible explanation for this confusion (1). The old American Code name for *Potentilla anserina* is *Argentina Anserina* (L.) Rydb., and this fact possibly explains why *Potentilla argentea* has been collected by some who thought the two plants were identical. The American Code of naming plants followed by Rydberg, Small, Britton and Brown, and others was ruled out at the last meeting of the International Botanical Congress, the type species being alone continued.

Although *Potentilla anserina* is listed as occurring from New Jersey northward and westward (2), it appeared impossible to secure an unadulterated supply from domestic sources. (During the week of July 9, 1939, Dr. Youngken (5) reported that he saw *Potentilla anserina* in fair amounts growing in gravelly soil along the Aroostook and Rustic Rivers in Aroostook County, Maine.) After 14 months, S. B. Penick and Company was finally successful in securing an authentic lot from a foreign source. The identity of this lot was confirmed by Dr. Youngken.

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The literature has disclosed very few references on the action of *Potentilla anserina*. Maisch (3), in a paper entitled "On the Constituents and Properties of the Genus *Potentilla*," states: "*Potentilla anserina* L. (Silver Weed). Both the herb and perennial root have a mild astringent taste, and are said to have been used by the Indians as an antidote to snake poison; while in Europe it was employed in diarrhea, hemorrhages, pulmonary complaints, some hepatic disorders and dropsy." Le Maout and Decaisne (4) simply state: "Roots and Leaves astringent."

On the basis of animal experiments in which muscular cramps artificially produced by barium were relieved by *Potentilla anserina* (7), Hauptstein (6) tried the drug clinically in dysmenorrhea. Capsules containing 0.25 and 0.5 Gm. were given three times a day, one, two or three capsules at a time, from two to three days before menstruation through the first part of the period. Pain was prevented in several cases, but generally only for the period during which the drug was administered. In a few cases, however, dysmenorrhea seemed permanently cured by treatment with the drug before and during a single period. Failure was reported only in one case of a hypoplastic uterus, one myoma case and 2 cases where the anatomical findings were negative. Hauptstein recommended the drug because of its cheapness and low toxicity.

For the sake of clarity, Beckman's (8) practical statements concerning essential dysmenorrhea are introduced here. "*Essential Dysmenorrhea* (Painful Menstruation): Perhaps more than 50 per cent of women suffer from dysmenorrhea, the symptoms varying from a mild physical and mental discomfort that is little greater than the normal depression during the period, to severe attacks of pain that rack the patient's back, head, legs and lower abdomen for several days and leave her in a state of great fatigue during the early part of the intermenstrual period. Grant that dysmenorrhea is only a symptom and not a disease, and classify the various types on an alleged causative basis, the fact will remain that there is a constitutional something under-

lying all the cases; that is to say, that the dysmenorrheic woman differs in some essential way from the nondysmenorrheic. This position is of course challenged, and the attempt is made to find a neuralgic, ovarian, congestive, obstructive, inflammatory, mechanical, autonomic, endocrine or allergic cause in all cases—which would be very fine were it not for the fact that the very same *causes* are found in many individuals who do not have dysmenorrhea. Therefore, in the present state of our knowledge, the term 'essential dysmenorrhea' would seem to be permissible."

EXPERIMENTAL

Material Used.—An extract, representing four times the concentration of the dried crude drug, was manufactured from the dried authentic *Potentilla anserina*. Compressed tablets, each containing three grains of the extract, were manufactured from this extract of *Potentilla anserina*. No other vegetable, animal or chemical physiologically active drugs were added to the extract or to the tablets, and the tablets were not coated. Each of these compressed tablets of Extract of *Potentilla anserina* (3 grains) represented 12 grains of the powdered drug.

Toxicity Experiments on Animals.—Doses of from 4 to 8 tablets were administered to adult albino rats, guinea pigs and rabbits over a period of 10 to 14 days. These doses represented from 48 grains to 96 grains of the powdered crude drug, and from 12 grains to 24 grains of the Extract of *Potentilla anserina;* the maximum dose administered to human subjects by Hauptstein (6) being 24 grains of the powdered crude drug 3 times a day.

There was no evidence of any harmful effects on any of the experimental animals, and autopsies failed to disclose any deleterious effects on any of the internal structures of the animals. In fact, the animals would eat the tablets voluntarily, and did not appear to develop any dislike for food with which crushed tablets had been mixed.

The work of Schneider and Nevinny (7) was confirmed by these authors, using guinea pigs as the experimental animals.

Investigations on Human Subjects.—Two staff members took two tablets three times a day for four days without any evidence of ill effects, before the clinical studies on patients were started.

Eight physicians coöperated in making a clinical study of the Compressed Tablets of Extract of *Potentilla anserina*. These gentlemen were provided with a supply of the Compressed Tablets, and were sent the information set forth above.

Each physician's attention was called also to the following: "This drug is commonly known as 'Silver Weed.' You will note that Hauptstein (6) used from 4 to 8 grains in each capsule, and that the dose was given 3 times a day, and varied from 1 to 3 capsules. It appeared to us that this was rather bulky, and therefore we decided on an extract of the drug which represents 4 times the activity of the crude drug; thus, decreasing the actual bulk by about one-fourth. In short, the dose of the extract is then $1^1/_2$ grains (representing 6 grains of the drug) to 6 grains (representing 24 grains of the drug), 3 times a day. The tablets of the extract which have been made up are 3-grain tablets, and consequently, the *average dose* of the extract would be *from $^1/_2$ to 1 tablet*, 3 times a day. The *maximum dose* as given by Hauptstein (6) was 24 grains of the powdered drug 3 times a day (3 capsules each containing 8 grains of the powdered drug). Two of the tablets of the extract represent 24 grains of the powdered drug.

"It is interesting to note, in view of the prolonged delay (something over a year) in getting any material from Germany (or elsewhere), that one of the German firms (9) has just recently come out with a preparation of this drug. This manufacturer claims that clinical tests are in agreement with the results of animal experimentation; that the drug is safe and sure with all spastic dysmenorrheal conditions; that with the majority of dysmenorrheal cases a quick and positive effect is obtained; that there are no side effects; and that even in large doses the drug may be used without hesitation. They advise using the drug several days before the period, but that even if the period has started the drug will give prompt relief from pain."

Clinical Results Observed.—After a period of several months had elapsed, each collaborating physician was provided with an adequate supply of forms similar to the copy which follows, with the request to return the same as soon as possible.

Clinical Data on *Potentilla Anserina*

1. Patients name, initials or number:_____
2. Age:____ 3. Social state: (*a*) S____ (*b*) M____ (*c*) W____
4. Has patient ever been pregnant____ Number of pregnancies____
5. Age at onset of menses____ 6. Frequency of periods____
7. Are periods regular____ irregular____
8. Number of days of average flow____
9. Severity of pain: (*a*) mild and continues work____ (*b*) moderately severe but continues work____ (*c*) forced to quit work or to go to bed____
10. On what day of period is pain most severe____
11. Results obtained with *Potentilla anserina:*
    (*a*) complete relief_____
    (*b*) partial relief_____
    (*c*) no relief_____
12. Were there any untoward or disagreeable side effects from the drug____ If yes, describe, briefly_____

13. Dosage and frequency of administration_____
14. Total number of tablets given____
15. Physician's name or initials_____

From the foregoing data, the following summary of the same is of interest:

Number of patients studied: 25.
Single: 15; Married: 8; Widows: 2.
Number who had been pregnant: 3.
Number with irregular periods: 8.
Number with regular periods: 17.
Number having mild pain and continue work: 2.
Number having severe pain but continue work: 7.
Number forced to quit work or go to bed: 16.
Number showing complete relief after *Potentilla anserina:* 8.
Number showing partial relief: 14.
Number showing no relief: 3.
Number showing side effects: 2 with dryness of mouth; 1 sleepy; 2 nausea, but probably not due to drug.
Dosage: 1/2 tablet: 3; 1 tablet: 17; 2 tablets: 5.
Total number of tablets taken: 1 1/2: 1; 6: 2; 9: 1; 12: 15; more than 20: 6.

The three social states were represented; also patients who had been pregnant. Sixty-eight per cent of the patients were regular, and 32% were irregular. Four per cent had mild pain but continued work; 32% had severe pain but continued work; and 64% were forced to quit work or to go to bed. Of these patients 32% were completely (one "almost completely") relieved of discomfort and pain; 56% were partially relieved; and 12% showed no relief (one of these three patients later showed pathology of the cervix).

From what is known of the action of *Potentilla anserina*, it is probable that the dryness of the mouth mentioned by two patients, the sleepy feeling mentioned by one patient and the nausea referred to by two patients were not due to *Potentilla anserina*, but were probably psychic.

It is to be noted that the single dose ranged from 1/2 tablet to 2 tablets, and it is possible that some of the patients who were only partially relieved of discomfort and pain might have been completely relieved with larger dosage; this might be true also of 2 of the 3 unrelieved patients. It is regrettable that a larger supply of tablets were not available so that this point might have been definitely established.

Patients took from a total of 1 1/2 tablets to as many as 40 tablets. This gave opportunity for observance of patients who had been on *Potentilla anserina* for longer periods. As yet, the time of experimentation has prohibited adequate observations which would warrant any statement as to the possibility of permanent cures. It is obvious, however, that in 88% of the patients either complete (32%) or partial (56%) relief was obtained. From the data presented it is obvious, too, that *Potentilla anserina* is of material use for relieving the pain and discomfort which may attend the condition under discussion, without the aid of any other drug agents. The obvious advantages of this fact need no comment, although combinations with other drugs might be resorted to in certain cases. Although the work completed has not established the probability of permanent relief, the advantages of having a non-narcotic, non-coal-tar agent for such application are great indeed. Many of the physicians and still more of the patients are desirous of securing additional supplies of the agent. Calls for the tablets continue to come in from the collaborating physicians, as well as from physicians who have not used the drug but have heard of it during casual conversations with the men who have experimented with the tablets. Some of them have said that even in the event *Potentilla anserina* is not a permanent cure, nevertheless the relief afforded even temporarily (during menstruation periods) warrants its existence and use, for some of these patients who have been relieved by *Potentilla anserina* heretofore got relief only from a hypodermic injection of one of the narcotic drugs.

Further clinical investigations are being carried out in two of the larger medical centers of the country. An investigation of the constituents of *Potentilla anserina* is under way. The authors wish to express their thanks to Dr. Heber W. Youngken for his valuable assistance.

REFERENCES

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NOTICE

Delays in publication are frequently due to the fact that authors fail to carefully check the list of references. The editor cannot be expected to supply missing parts of references.