

ANTHRAQUINONE CONTENT OF WORMY RHUBARB.*

BY A. A. MAIER AND C. W. BALLARD.

Supplies of rhubarb showing the effects of insect attack are occasionally received and the question regarding the therapeutic activity of such material was raised by a dealer. His query was based upon the proposition that wormy belladonna root and aconite frequently contain relatively more alkaloid than sound materials owing to the fact that starch is consumed by the insect. Reasoning from this argument and if this condition obtains in rhubarb, wormy material should be more active therapeutically than sound drug. The use of materials showing the effects of insect attack is rightly prohibited by the U. S. Pharmacopœia and National Formulary. That such materials can be and are used for the extraction of alkaloids is admitted, but when so used practically all possibilities of insect contamination in the finished product are eliminated. Whether or not the same would hold for galenical preparations manufactured from wormy rhubarb is an open question. Undoubtedly there is danger in too freely admitting wormy materials for manufacturing purposes and in each instance permission should be withheld until it can be conclusively demonstrated that all traces of insect contamination are removed during manufacture.

The rhubarbs used in this work were examined microscopically (by C. W. Ballard) and chemically (by A. A. Maier). As the chief point in question was the determination of therapeutic activity as indicated by the anthraquinone content of the wormy material, the chemical examinations were more extensive than the microscopical.

MICROSCOPICAL EXAMINATION. •

Sample A.—This represented a commercial sample of whole sound root and was used for comparison purposes. Microexamination of this sample showed the usual histological characters of rhubarb root and showed no evidences of insect attack.

Sample B.—This sample represents a shipment which was rejected because of insect infection. While fragments of the root showed numerous borings they were fairly firm and the fracture was but slightly different from sound root. The powdered sample is dark orange-brown in color and within the color range of sound rhubarb. Microscopical examination of this powder showed insect webbing and fragments of insects. It contains smaller amounts of starch and larger amounts of fibrovascular tissues, parenchyma and calcium oxalate crystals than a normal sample.

Sample C.—This lot represents those portions of Shipment B in which insect infection was most marked. The color of the powdered material is a dark orange-brown and but little different from the color of Sample B. Microscopical examination showed still further reduction in the amounts of starch and increase in the amounts of fibrovascular tissues, parenchyma and calcium oxalate crystals than noted in connection with Sample B.

Sample D.—This sample of rhubarb was obtained from the college drug collection, being a museum exhibit to show the ravages of insects. It was so com-

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pletely worm-eaten that it crumbled upon the slightest pressure. The powdered material was of a dull brown color and of fibrous texture. Microscopical examination showed large amounts of insect remains and webbing. This sample showed the same characters as Sample C, merely differing in degree—starch being still further diminished and the fibrovascular elements, parenchyma and crystals, being greater in amount.

Sample E.—This material represents the dust deposited in the jar containing Sample D. It was a fine powder of very dark brown color. Microscopical examination showed that it consisted almost entirely of insect remains. Moderate amounts of the characteristic calcium oxalate crystals of rhubarb were present together with very few starch grains and but traces of the other tissue elements.

CHEMICAL EXAMINATION.

This work consists in assaying material in various stages of worm infestation by the gravimetric method of Vanderkleed, for anthraquinone content. The samples ranged from sound to completely worm-eaten material. The following table shows the anthraquinone percentages found in the above samples:

Sample.	A.	B.	C.	D.	E.
1st.....	1.45	2.48	1.30	1.04	0.98
2nd.....	1.25	2.29	1.05	1.12	1.09
Average.....	1.35	2.38	1.17	1.08	1.03

Administration of 0.5-gram doses of whole wormy rhubarb root and similar quantities of particularly wormy portions of such a root gave greater laxative effects than 0.5-gram doses of a sound rhubarb root. It has been noticed that the whole wormy root possesses greater laxative properties than selected wormy parts.

From this experience it would appear that the insect attack causes a relative increase in anthraquinone content. The extent of this increase is subject to great variation but it was noted that there is a limit in insect infection beyond which there is a diminishing of the anthraquinone content. After this turning point it is probable that changes incidental to decomposition play a part in the apparent loss of anthraquinones. However, the laxative properties seem never to be entirely lost even in very old and wormy materials.

In work of this kind comparisons should be restricted to the same variety because of the great variation in oxymethylantraquinone content in different commercial grades. Tschirch and Heuberger have found this to range from 1.2% to 3.3% and state that a variety may be recognized by its percentage.¹

One may ask the old question as to what the active principle of rhubarb really is. Tschirch and Heuberger claimed that it contains no resin, the purgative action being due to anthraglucosides and derivatives (meaning that the constituents are emodin, rehin and chrysophanic acid).² This the writer believes to be correct.

Tschirch's colorimetric and Vanderkleed's assay schemes were found to have the faults of any "shake out" method. In addition, the color comparisons should be made within two or three days after extraction as precipitation and destruction of the cherry-red color occur upon standing. Also, in Vanderkleed's method in

¹ *Proc. A. Ph. A.*, 52, 658, 1904.

² *Ibid.*, 51, 733, 1903.

the final extraction, great care must be taken to exclude sulphuric acid from the residue since very small amounts will, after concentration by the evaporation, destroy the residue.

It is evident that an improved method of assay or standardization for rhubarb root would be a means of eliminating unfit material and of securing a drug of uniform therapeutic activity.

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TOXIC PROPERTIES OF DIETHYLPHTHALATE.

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In an excellent paper on diethylphthalate,* Handy and Hoyt mention one experiment to show its toxic properties. The following tests show that this ester has little or no toxic properties.

A number of white rats were given *per ora* doses up to 0.5% of their body weight. The larger doses caused considerable pain, weakness and great distress for a period of ten or twelve hours; after about twenty-four hours the behavior of the animals was normal. A female rat was given 0.5% of her body weight twice while pregnant, the last time a week before delivery, yet she gave birth to a normal litter of young and all were healthy animals.

To one-year old leghorn pullets doses up to 1.5% of the body weight were administered *per ora*. The birds were not as badly affected as the rats. About six hours after feeding they showed the effect of the ester in being unable to walk but after twelve hours they were normal again. Nothing was gained by increasing the dose as the oil was excreted unchanged.

Apparently the oil is but slightly absorbed by the skin and the portion that goes into the body has little action. Laborers manufacturing diethylphthalate have their hands in the oil and their clothes saturated, in places, for days at a time and notice no effect whatsoever. One case in particular was that of a worker repairing a still who had spilled on his back hot oil sufficient to saturate his under and outer-shirt. He worked the whole day in this condition without any irritation, nor was he affected in any way as far as he could ascertain.

But when brought into contact with the mucous membranes as of the eyes and mouth especially in the presence of alcohol a very severe burning, fiery sensation is produced for some time or until the oil is removed. Only the slightest inflammation or redness is produced, and this disappears immediately on the removal of the oil.

These experiments indicate that diethylphthalate present in denatured alcohol has no deleterious action on the skin and is probably non-toxic to humans.

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* JOUR. A. PH. A., pp. 600-609 and 702-710.