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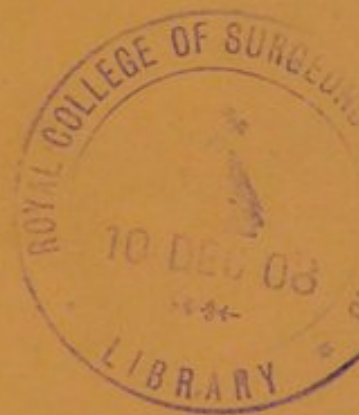


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SOME time ago I received from Kew by the direction of Sir W. Thiselton-Dyer a small package of seeds which had been sent by Mr J. H. Hart of the Botanical Department, Trinidad. These seeds are derived from an Euphorbiaceous plant now recognised by Mr Hart as the *Garcia nutans*. Larger samples have been sent to me more recently from Trinidad of the seeds of two *Omphaleas* which though belonging to the same natural order are of different species from the *Garcia nutans*. These are named respectively the *Omphalea triandra* (this is called "Cob-nut" in Jamaica) and the *Omphalea megacarpa* or *diandra*. Mr Hart, who has sent me further samples of these seeds, though he has been unable to obtain more of the *Garcia nutans*, informs me that in the fresh state all of them possess a laxative action and that they have been occasionally employed dietetically in Jamaica for this reason.

It is proposed in this paper to give a brief account of the action of each of these seeds in the fresh condition as well as of their contained oils upon man and certain of the lower animals. As the amount of material was limited a satisfactory examination in order to demonstrate the possible presence of other principles was not practicable, and therefore this report, though justified by the facts established, is incomplete in this respect.

SEED OF GARCIA NUTANS.

The seed (Fig. 1) is oval and obscurely beaked, convex on both dorsal and ventral surfaces, but more so on the former, which shows a well-marked median raphe passing backwards from the beak at the micropyle. On the ventral surface is a well-defined hilum of triangular form with its base directed towards the micropyle. The testa which though thin is hard and resistant has a buff ground colour splashed with irregular light-red to rusty brown patches. The seeds in the small sample showed a striking uniformity in size. Of the 15 seeds examined the average length was 16 mm. The variation between longest and shortest was only 2.5 mm. The average width was 12.5 mm. Variation frequently

inversely to length. The average weight was 1.107 grm. The greatest variation from the average was by .164 grm. Within the testa and underlying thin papyraceous tegmen, the erect embryo with broad cotyledons is found enclosed by an abundant endosperm fully occupying the cavity. The average weight of the seed deprived of its coverings was .792 grm.

The odour of the freshly broken seed is nut-like and agreeable, on chewing a fragment the corresponding taste is accompanied by a sensation suggesting the presence of oil, but soon an unpleasant tickling or scratching manifests itself chiefly in the velar and pharyngeal regions. Other subjective symptoms, to be described later, appear after a longer interval.

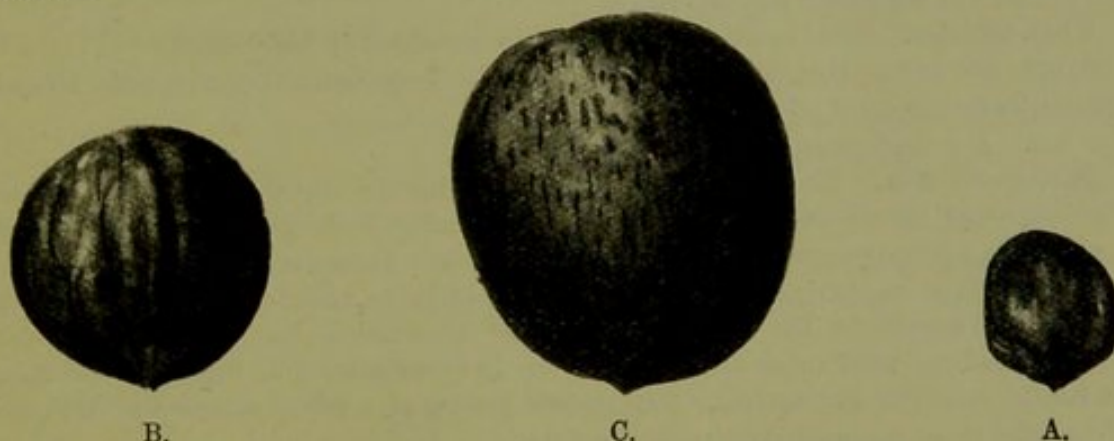


Fig. 1. Seeds natural size. A. *Garcia nutans*, lateral aspect; B. *Omphalea triandra*, dorsal aspect; C. *Omphalea diandra*, dorsal aspect.

When a fragment of the kernel is rubbed with mucilage of gum acacia a rich white emulsion results, indicating the presence of an oil. Prolonged extraction by ether of the seeds which have been previously thoroughly reduced in the mortar shows the proportion of this oil to be considerable. The mean of two estimations was 36.29 % of the kernel weight or 26 % of the seed with coverings intact. This oil is at first of a pale straw yellow colour, clear and limpid, but within a few weeks of its separation gelatinous flakes appear and these rapidly increasing the whole of the oil is converted into a translucent gelatine-like mass. Or if exposed to the air more or less lardaceous material is developed in association with the translucent portion. Whether the body formed is a metameride of the original oil, or otherwise, is undetermined. It is in the altered state insoluble in ether, and appears to be much reduced in activity.

The material at disposal therefore consisted of (a) the fresh seed, (b) the ether extracted oil, (c) the residual whitish powder.

(a) *The fresh seed of Garcia nutans.*

Action on man. A healthy adult leading an uniform life on an average mixed dietary undertook the consumption of the seeds, etc. and

the registration of results (as this individual had a single evacuation at the same hour daily, under usual conditions, he was regarded as a favourable subject for such observations). A few of his experiences will be transcribed here :

No. 1 Obs. At 12 a.m. (four hours after breakfast) .6 gm. of the fresh seed, deprived of integuments, was chewed to a fine pulp which was swallowed, thereafter 20 c.c. of water were used to rinse the mouth so that all the particles adhering to the teeth were conveyed to the stomach. A few minutes after swallowing a slight tickling or scratching was noticed in the region of the fauces and soft palate.

2 hrs. 30 mins. Some gastric discomfort soon succeeded by borborygmi.

5 hrs. 20 mins. One alvine evacuation with discomfort. Dejecta partly formed. Apparently no excess of bile or mucous.

9 hrs. A second evacuation of similar character.

Subsequent note. There was no disturbance during the night. At 8 a.m. (20 hours after ingestion) on the succeeding day, a little discomfort in the gastric region being still present, one evacuation, more formed. The discomfort disappeared in the course of the morning but the evacuation of the day following (44 hours after ingestion) was of a soft character. Throughout the earlier part of the observation there was slight vesical irritation and the total urine measured for the 24 hours succeeding ingestion, was about 230 c.c. in excess of the normal. The specific gravity of a mixed sample was 1015, the colour pale, there was no deposit upon standing.

No. 2 Obs. A week after the last experiment, the condition of the observer being quite normal, .4 gm. of fresh seed was taken.

105 mins. Slight gastric discomfort.

180 mins. Borborygmi, feeling of warmth in right iliac region.

6 hrs. One evacuation, soft but formed, urine increased.

20 hrs. At usual time, one evacuation of like character. There was no further disturbance.

No. 3 Obs. Ingestion of .2 gm. of fresh seed was followed by a formed but soft evacuation in usual course on the ensuing morning.

No. 4 Obs. .1 gm. produced no independent action but the next customary evacuation was in two out of four observations of a somewhat soft consistency.

It is evident from these as well as from other experiments which are not detailed here, that an action both powerful, prolonged and associated with some griping may follow the free employment of the fresh seed of *Garcia nutans*, and equally that by reducing the dose a sure but simple purgative or laxative effect may be the limit of action. Renal irritation with resulting diuresis (probably occasioned during elimination) is not witnessed after small doses. The purgative action of the seed may be further exemplified by reference to its therapeutical employment in a single case.

The patient, an adult female, was suffering from disturbance of the alimentary canal after partaking of indigestible food. The tongue was unduly red, the pulse accelerated. .5 gm. of the fresh seed of *Garcia nutans* (well reduced) was administered with two

mouthfuls of water. In 2 hrs. 30 mins. slight discomfort was experienced and during the ensuing 3 hrs. 30 mins. three soft evacuations were passed. The alimentary and concomitant symptoms subsided after purgation.

Summary of action of ingested seed upon rabbits and mice. Both rabbits and mice ate, with avidity, portions of seeds presented to them. Purgation, varying in degree with the amount consumed, followed after a time interval. If the amount ingested was relatively large, the dejecta were semifluid and contained much mucous; if small, the dejecta were formed though soft in character. The ingestion of .3 gm. by a rabbit caused active purgation in 70 mins. and again in 130 mins. A similar result in the main followed the introduction of a like amount triturated with gum acacia through an œsophageal catheter into the stomach of a rabbit, which was temporarily anæsthetised by nitrous oxide gas; some mitigation of action in this instance may be attributed to the presence of the mucilage: .02 gm. of the seed and even less caused active purgation in mice.

Effect on peristalsis. In order to ascertain the action of *Garcia nutans* seed on intestinal peristalsis, it appeared desirable to register the movement of the viscera. Etherised cats were employed for these experiments. One vagus and one splanchnic nerve were exposed in their thoracic course, ligatured and the distal ends placed upon insulated electrodes. Two fine gum elastic catheters terminated by compressible rubber bags were introduced into the intestinal lumen, one being passed from the stomach into the duodenum, the other from the jejunum upwards into the lower duodenal or upper jejunal region, so that their compressible portions lay some 8 cm. apart. The sounds were secured in position by suture at the point of introduction. Insulated electrodes were attached to the suprarenal bodies. Blood pressure was recorded from the left carotid artery. The bags and sounds were lightly charged with water and thereafter brought into connection with a system of water-containing tubes which terminated in two delicate recording mercurial manometers. The body temperature was maintained by means of a warm trough. The effect produced by stimulating thoracic vagus and splanchnic was then tested. If vagus stimulation caused the appearance of slight peristaltic contractions, or when (which was also only exceptionally the case) faint contraction of the circular muscular fibres appeared spontaneously, both splanchnic and suprarenal stimulation suspended the movement. After these preliminaries, emulsion of *Garcia nutans* seed was carried either into the stomach by means of an œsophageal tube or into the duodenum by way of the pyloric orifice.

Exp. Fully etherised animal. Preparation as above. (The stomach contained a little nearly digested food.) The intestine was quiescent. Result of peripheral vagus stimulation on intestinal wall, faint contraction on two, negative on three occasions. Injection into the stomach of .4 grm. of emulsified seed of *Garcia nutans* was speedily followed by spontaneous movement of the walls of the duodenum which after continuing for 12 mins. gradually disappeared. The original condition of quiescence having been restored injection of a similar dose of emulsified seed was made through the pylorus directly into the duodenum. This was followed within 2 mins. by powerful contractions involving both duodenum and the upper part of the jejunum (in which the lower bag was situated 8 cm. below the upper), the waves of peristalsis started below the pylorus rapidly traversing the section of intestine separating the points of observation. (Some of these contractions were of a greatly prolonged character and contrasted markedly both in strength and duration with the slight contractions which had twice followed vagus stimulation, Fig. 2.) This condition of local excitement, which was controlled by splanchnic stimulation, began to decline in 15 mins. but for a much longer time it was present in degree, whilst vagus stimulation was distinctly effective in causing its reappearance.

As has been mentioned the movements were, even at their most active stage, temporarily suspended by splanchnic stimulation, and this is equally the case when the stimulation was suprarenal. There was no important modification of the blood-pressure for the first hour (during which time the tracing was of course taken) after injection of the emulsified seed.

This experiment embodies the chief results of the remainder, which however showed that peristalsis is induced by *garcia nut* and thereafter by vagus stimulation alike in the fed and unfed condition of the animal. These facts suggest that a local action of the purgative upon the afferent nerves of the mucosa is translated by the stimulation of the intramural nervous plexuses into a progressive peristaltic movement, which is controlled by sympathetic excitation. The effect did not exist long in its most active form in any one part of the intestine, but as the movement induced transfers the irritant to another portion of the tube more remote from the pylorus the excitement is developed in a lower section as it declines in the upper. Probably the enhanced secretion which results from local action of *garcia seed* will serve to reduce the degree of irritation as the passage through the intestine becomes lengthened. It is possible that the anæsthetic employed tends from the first to reduce the degree of response to a local stimulation. No contraction occurred in the rectal portion of the large intestine during the active contraction provoked in duodenum and upper jejunum (Fig. 2). On subsequently examining the lining of the intestine which had been exposed to the local action of *Garcia nutans seed*, no evidence of inflammatory action or other alteration in the mucosa could be detected.

In order to ascertain what modification is produced in the speed of intestinal peristalsis after *Garcia nutans*, I employed the method which

I have previously described (*Proc. Roy. Soc.* XLI. p. 215. 1886). A Vellas fistula had been established in this dog some months previously, the two ends of the isolated loop of intestine (jejunum) being healed into the linea alba. The animal was in all respects in excellent condition,

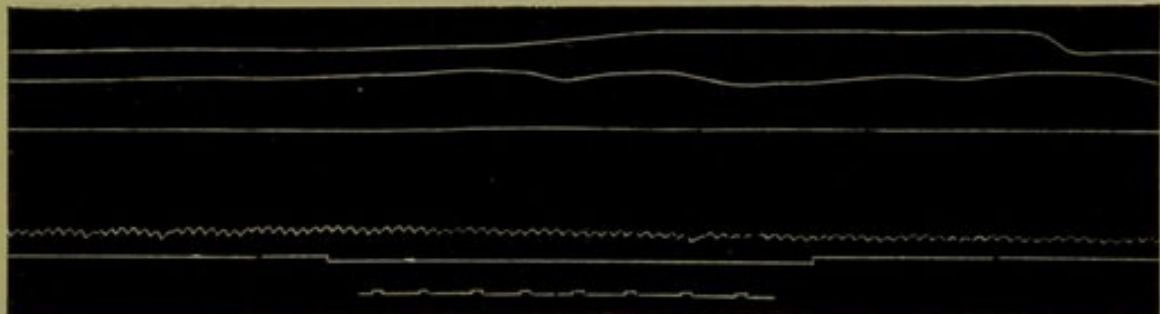


Fig. 2. Spontaneous movement of intestinal wall after introduction of *G. nutans* into upper end of duodenum. The top line is recorded from the duodenum, the second from the jejunum, the third from the rectum. The signal indicates duration of splanchnic stimulation. The pulse and pressure recorded above by Fick's spring manometer. Time is indicated below in two second intervals.

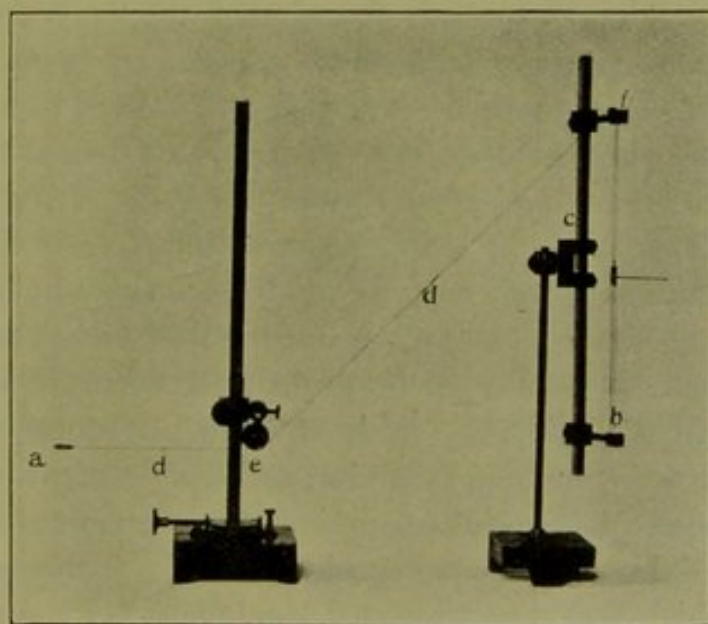


Fig. 3.

it was exercised daily and was keen for its food. When laid on its side upon the table it would usually retain its position throughout the observation without any restraint, but if excited by a sudden noise or the entrance of a stranger it was necessary to lay a hand on the shoulder or thorax to tranquillize it. The experiment consisted in noting or recording the speed at which a small ivory sound (Fig. 3 *a*), somewhat egg-shaped, passed through the loop of intestine, before and after the introduction

of emulsion of *Garcia nutans* seed. This travelling sound, which is perforated for attachment to a thread at one extremity, is 8 mm. long by 4 at its greatest width. The graphic apparatus consists of two fine parallel steel wires (*b.b.*) tightly braced upon a brass frame (*c*) which is itself adjustable upon the upright bar. This bar, which has tangential movement, is fitted upon a heavily footed stand. On the parallel wires which act as guides a very light ivory frame, bearing a registering bristle moves vertically without friction. The silk thread (*d*) connected with the travelling sound passes over the grooved edge of a freely moving wheel and thence to a similar but much smaller (1 cm. diam.) wheel (*f*) placed between the upper attachments of the parallel wires. After passing over this wheel it is secured to the light movable frame which is immediately below its grooved margin.

When traction is made through the medium of the thread, as by the passage of the travelling sound into the intestinal loop, the ivory frame is raised, the point attached drawing an upward curve upon a recording surface moving slowly in front of it. The animal having been placed on its side, the abdomen towards the edge of the flanged wheel (*e*), the travelling sound was introduced into the upper opening (in the physiological sense) of the loop, the level of the wheel adjusted so as to tense the thread and bring the recording frame into position over the time marker. A record was then obtained of the speed of transit of the sound under existing conditions, whether of hunger or satiety. Immediately after, a measured amount of *Garcia nutans* seed was gently injected into the upper opening of the loop, and after a noted time had elapsed the sound was again introduced and a second transit recorded. Simple observation showed that in 2 mins. to 3 mins. after the introduction of the emulsion, both mouths of the loop exhibited active movement, and that from the lower a largely increased amount of clear intestinal fluid was extruded. This fluid soon became turbid from the presence of emulsion, a portion of which had thus traversed the length (11.5 cm.) of the loop. Though the approach or odour of food produced an increased secretion when the animal was hungry, the separation which ensued upon the local action of *Garcia nutans* was much greater.

The following notes illustrate the modification in peristaltic propulsion occasioned by local contact of the emulsion.

Obs. 8 (Fig. 4 A and B). 9 a.m., animal fed 20 mins. ago. The sound traversed the loop and was expelled from the lower orifice in 8 mins. 45 secs. A mucilaginous emulsion of .15 gm. of the seed was at once introduced just within the upper opening of the loop and 4 mins. thereafter the sound was reinserted. Active pendulum movements of the loop

without propulsion for 2 mins. 10 secs. thereafter powerful coordinate peristalsis, the transit being now completed in 5 mins. 10 secs. or in 3 mins. 35 secs. less than in the control observation. The length of the loop was 11.5 cm., so that discounting the time before coordinate movement commenced an average of 15.6 seconds per cm. is attained whilst the speed in the control was 1 cm. in 45.6 seconds.

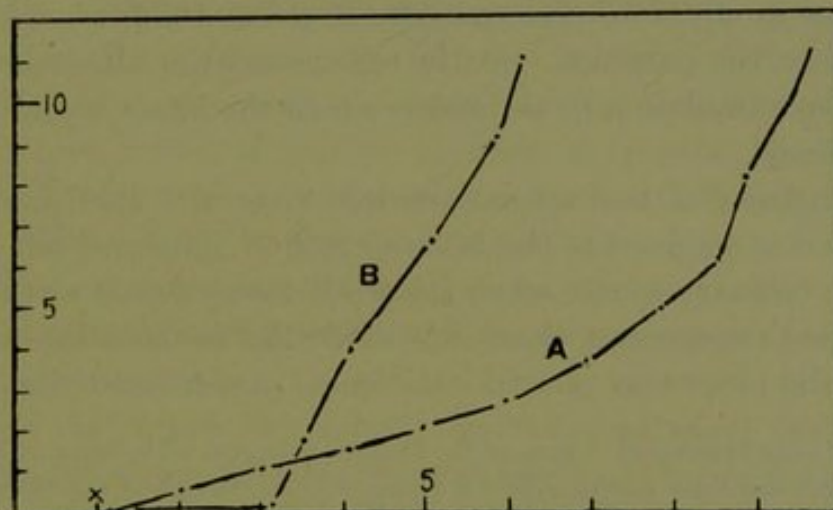


Fig. 4. Peristaltic propulsion of sound in the intestine. One division of the abscissæ = 1 min., one division of ordinate line = 1 cm. of intestine traversed. A. 20 mins. after food. B. 10 mins. after completion of A, and 4 mins. after introduction of *Garcia nutans* seed (emulsified). Pendulum movements occur in B before active propulsion commences. Sound introduced at X.

Obs. 10 (Fig. 5 A and B). The animal fed 80 mins. ago. Peristalsis moderate but steady, the sound making the journey in 12 mins. 4 minutes after the introduction of .1 gm. emulsified seed marked increase of secretion which with some emulsion is extruded from the lower opening. On inserting the sound (6 mins.) active propagating contractions with some "pendulum movements" were recorded, expulsion taking place in 5 mins. 15 secs. The speed of transit was therefore more than doubled. The time per 1 cm. traversed is 27.4 secs. before, and 62.6 secs. after introduction of *Garcia nutans* seed.

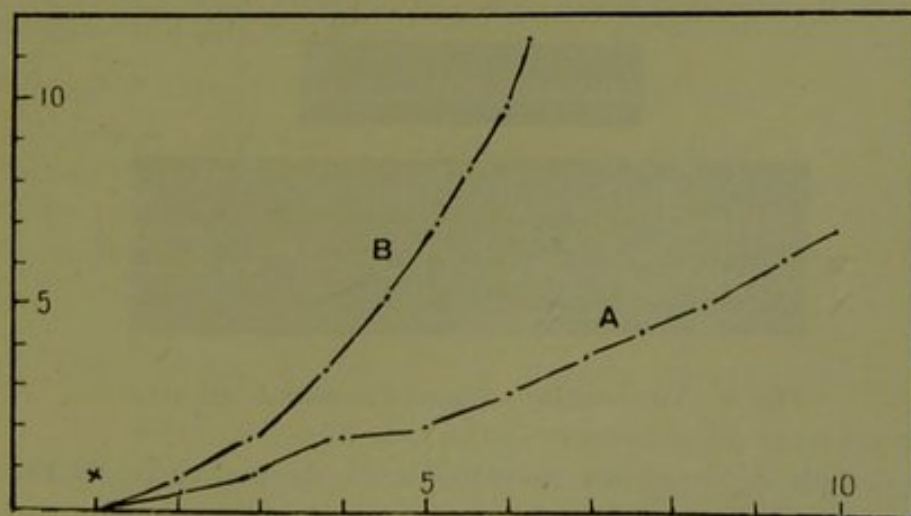


Fig. 5. Peristaltic propulsion of sound in the intestine. Values as in Fig. 4. A. 80 mins. after food. The sound traversed the loop in 12 mins. B. Taken 10 mins. after completion of A and 4 mins. after introduction of *Garcia nutans* seed (emulsified).

Whilst local excitement in the loop of intestine is distinctly abating in 15 to 20 mins. after introduction of the emulsion, some residue of it is observed for much longer, frequently for $2\frac{1}{2}$ to 3 hours. Local anæsthetics such as cocaine and very weak solutions of the members of the aconitine group (*Phil. Trans.* CXCv. B. p. 72. 1902) when introduced shortly before the emulsion, greatly reduce or even altogether prevent the effective stimulation to peristalsis which the latter would otherwise have occasioned.

No purgation of the animal resulted from the emulsion when its application was confined to the isolated loop of intestine, but purgation followed in ordinary course when the fresh reduced seed was swallowed. The following experiment shows how little the isolated intestine participates in the otherwise general excitement under such circumstances.

The unfed animal received .3 gm. of the seed incorporated with 5 gm. of beef fat. In two hours there was some restlessness, for borborygmi were frequent and the movement of the intestines was so active that it could be detected through the abdominal parietes. A record taken at this time showed no marked acceleration of peristaltic movement in the isolated loop, in fact the speed was almost identical with that recorded before the seed was swallowed. Active purgation occurred just as the observation terminated and was twice repeated at short intervals.

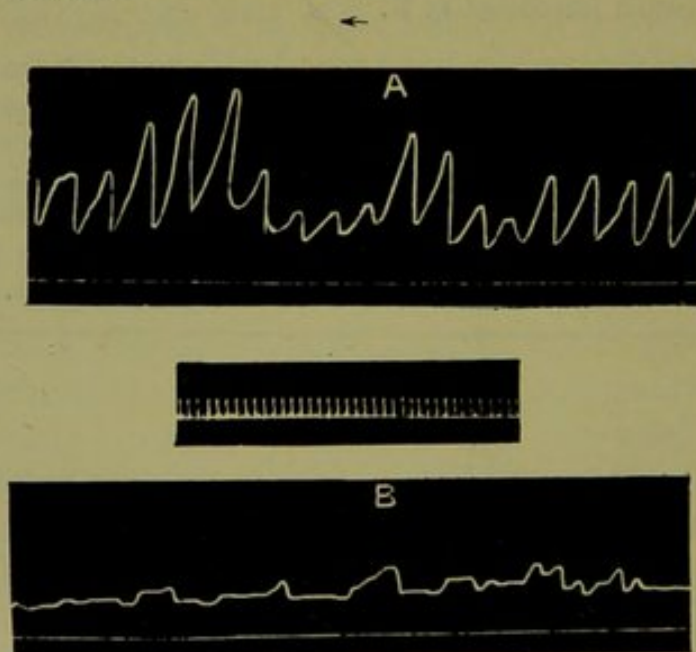


Fig. 6. Time marker registers two second intervals.

If a compressible sound is introduced deeply through the upper opening of the intestinal loop eight minutes after the introduction of emulsion of *Garcia nutans* seed, the record obtained shows, as might be anticipated from the experiments already described, very powerful and

enduring contractions in the first instance, recurring at fairly regular intervals (Fig. 6 A). The individual contractions (none of which are marked by respiratory impulses) last for five and six seconds. Some rolling or pendulum movements are twice recorded. In the second tracing (B) taken five minutes later the contractions of the circular muscular coat are much less energetic though they are long sustained, fifteen minutes later there were only occasional contractions at long intervals.

Action upon frogs. Injection of fresh emulsified seed of *Garcia nutans* into the stomach of decerebrated frogs is seldom followed by any purgative effect. After an hour's interval the organ is found to be energetically contracted round the emulsion and much mucous is found within its lumen. Small hæmorrhagic spots are exceptionally present in the mucous membrane.

Injection of .02 gm. or more of the fresh emulsified seed into the dorsal lymph sac of decerebrated frogs is followed by no evident irritation, but all reflex disappears in from 24 to 72 hours—occasionally .005 gm. may have a similar result. (There is much variation in the speed of the lethal issue, which further bears little relationship to the dose employed: occasionally there is cutaneous ulceration at the seat of injection.) Examination post-mortem shows the presence of a blood-tinged fluid in the dorsal sac, on the walls of which there are numerous hæmorrhagic points. The heart is arrested, but the ventricle responds feebly to electrical and mechanical stimulation (when reflex has just disappeared). Excitability of motor nerves and muscular tissue of the extremities is little, if at all, reduced.

Obs. 1. R. esc. of 38 grms. received .1 gm. of emulsified seed in dorsal lymph sac. No symptoms. Reflex disappeared in 44 hours.

Obs. 2. R. esc. of 30 grms. received .05 gm. as above. 23 hours.

Obs. 3. R. esc. of 27 grms. received .01 gm. as above. 62 hours.

In no instance was there purgation or any positive symptom. In all three the presence of hæmorrhagic points upon the walls of the dorsal sac was recognised. There was however no parallel appearance in stomach, intestines or elsewhere. In No. 3 there was slight cutaneous ulceration at the site of injection.

(b) *Action of the oil of Garcia nutans seed.*

Only a very small amount of the oil was available for experimental purposes and therefore the information regarding its action is incomplete. The results may be summarised as follows:—

On man. .4 gm. caused no discomfort but six hours after ingestion one soft evacuation with a similar effect on the morning following. This dose was repeated on three occasions with very similar results, thrice out of the four observations, sensation of warmth in the right iliac region four to five hours after injection is recorded.

.2 gm. on two occasions, negative; on a third, the morning evacuation on the succeeding day (15½ hours) was soft in character.

.1 gm. Result invariably negative.

On rabbits. A distinct purgative action followed doses of .6 gm. and a moderate effect was recorded after .4 gm. but no drastic catharsis resulted even from the larger amount.

The effect of the gelatinised or concrete oil was also tried.

On man. .6 gm. occasioned a formed evacuation in 6½ hours and a loose evacuation on the following morning (16½ hours).

3 gm. produced a slight laxative action on the morning succeeding ingestion. No discomfort resulted from these or similar doses, but on two occasions there was a sensation of warmth, as noted above.

On rabbits. Doses of .8 gm. were followed by a moderate purgative action, but the amount of urine was considerably augmented.

A fully grown animal (2100 grms.), having received for a week a daily dietary of 100 grms. fresh vegetables and 150 grms. corn and bran mixed with 100 c.c. water, totalled for three days before administration of oil; faeces 244 grms., urine 294 c.c., and for three days after administration of .8 gm. oil; faeces 294 grms., urine 432 c.c. The daily average before administration was therefore, faeces 81 grms., urine 98 c.c., and after administration, faeces 98 grms., urine 143 c.c. (On two occasions during the last triurnal period the faeces were very soft in consistency.)

Action of fresh seed of Garcia nutans contrasted with the oil. The irritant effect of the fresh seed is not occasioned by the oil (whether unaltered or altered in character) when given in corresponding doses, but a laxative or purgative effect is occasioned by the latter as well as by the former. But accepting the oily contents of the seed at 36.3% it is evident that the oil contained in .6 gm. of fresh seed (a dose which is distinctly purgative) would amount to .218 gm. Such a dose is occasionally laxative but is certainly far below the corresponding proportion of seed in activity. Even double the dose, which would correspond to nearly 1.2 grms. of seed, is much less active in causing purgation than .6 gm. of the seed has been found to be. Therefore the inference seems justified that some irritant principle which tends to cause discomfort, at the same

time increasing peristalsis and probably also incoördinate intestinal movement, is present in the fresh seed but is absent from the oil.

(c) *Action of the ether extracted residue of Garcia nutans seed.*

This residue, which consists of a fine greyish white powder devoid of greasiness and capable of reduction to an impalpable condition, produces discomfort in the abdominal viscera, impairment of appetite, and occasionally purgation in the human subject. Larger doses than 1 grm. were inadmissible in view of the fact stated in the next paragraph.

Action on frogs. Introduction of a very fine powder (no. 100) in quantities of .02 to .08 grm. well mixed with mucilage into the dorsal lymph sac of brainless frogs gives rise to abundant small hæmorrhages in the wall of the sac and even to ulceration of the skin (4—5 days) in proximity to the deposit of powder. Reflex disappears slowly even after large doses. Thus .1 was followed only on the fifth day by failure of reflex. Clearly a very irritant principle remains in the seed after the oil has been thoroughly extracted by ether.

Action upon mammalian intestine. These experiments were performed upon etherised animals (cats), the preparation being as already described, registration of contraction was through the medium of compressible sounds within the lumen of the intestine.

The dry ether extracted powder of *Garcia nutans* seed mixed with mucilage when injected into the stomach or duodenum, caused only slight increase of spontaneous movement of the intestine, but uniformly increased the effect of vagus stimulation (intrathoracic), so that in place of a purely negative result or feeble response previously witnessed, active peristalsis, though of no long continuance, was induced. No hæmorrhage or lesion of the mucous membrane was detected after ingestion of the powder.

The results recorded of the action of fresh seed of *Garcia nutans* and also of the ether extracted powder are suggestive of the presence of an irritant (possibly hæmolytic) principle, existing apart from the oil. The supply of material was unfortunately so nearly exhausted that though an attempt was made to isolate the body the result cannot be considered conclusive.

Twelve seeds deprived of their coverings were mashed up with 10 c.c. of distilled water and let stand for 18 hours. Filtration through fine swedish filter paper into 50 c.c. absolute alcohol followed. At once a white cloudy precipitate separated very slowly. Filtered, the filtrate was clear.

Redissolved the precipitate on the filter in 10 c.c. distilled water, reprecipitated with alcohol, on standing the precipitate gradually settled. The process was repeated and the precipitate was kept in absolute alcohol for six weeks. This method is described by Martin¹ as applied to the separation of the albumose of *Abrus precatorius* (jequirity).

A portion of the precipitate was removed in a pipette evaporated in the air and dissolved in a few drops of water. The solution was injected into the dorsal lymph sacs of two frogs. These died in three and five days respectively. Upon examination, identical appearances in the lymph sacs were detected, many hæmorrhagic points in the walls and a small amount of extravasated blood in the interior. The injections were repeated at the time with like results, but after standing for an additional six months the precipitate had almost completely lost its toxicity. A few seeds which had been in my possession for fully three years were treated by a similar method but failed to give the toxic effect when the precipitate from alcohol was dissolved in water and injected into frogs. Whether a toxalbumose (Martin) is actually present must therefore be considered undecided until another supply of fresh seeds is obtainable. If it should be established ultimately that the *Garcia nutans* seed contains such a body it will present a close analogy to the seeds of *Croton tiglium*, *Ricinus communis* and *Abrus precatorius*, all of which contain toxalbumoses.

SEED OF *OMPHALEA TRIANDRA*.

Mr Hart² states that whilst the plant bearing this seed is euphorbiaceous and of the same genus as the *Garcia nutans* and *Omphalea diandra*, it is of a different species from that embracing the former. He speaks of the seed as a sure but mild laxative. Dragendorff³ refers to the oil obtained from the seed of the omphaleas as purgative and employable in intestinal as well as in renal ailments.

Description. Although the width is slightly greater than the length, the seed is nearly spherical in form (Fig. 1, B). A faint beak is present at the micropyle from which three ill-defined ridges diverge and are lost on the sides. The testa is very hard and resistant, requiring a firm blow to break it. It is smooth and of a rusty or dullish mahogany tint often obscurely mottled with patches of a darker hue. Exceptionally it possesses a varnished appearance. The seed is light, floating buoyantly in water. Measurement and weight (ten seeds examined). Average length 22.86 mm. from beak to hilum

¹ *Proc. Roy. Soc.* XLVI. p. 101. 1890.

² Communicated.

³ *Heilpflanzen*, p. 384.

(largest 25.25, smallest 21 mm.). Average width 23.04 mm. (largest 25.8, smallest 20.5 mm.). There is therefore greater variation in width than in length. Average weight, 6.02 grms. (largest 6.22 grms., smallest 4.59 grms.).

Of the seeds contained in the sample 12 % rattled upon shaking. When deprived of the testa a variable amount of papyraceous tegmen is found enveloping the endosperm which has a faint creamy colour, smooth section, bean-like taste but no odour. The embryo is upright with broad cotyledons. The endosperm average per seed is 3.258 grms., the testa and tegmen weighing 1.747 grms.

An oily sensation is produced by the chewed seed, but there is no tickling or scratching sensation. Triturated with mucilage it yields a rich emulsion.

Of the reduced seeds, deprived of integuments, 30 grms. were weighed, thrice extracted with ether, the ether being subsequently evaporated at a low temperature. The resulting oil weighed 16.98 or approximately 17 grms. The total yield of oil is therefore 36.9 % for the seed intact or 56.6 % for the seed devoid of integuments.

The oil is of a pale yellow or straw colour, mobile and perfectly clear. It possesses a faint oleagenous odour, the taste is bland, nutty and agreeable. Its specific gravity is 0.924 at $\frac{15^{\circ} \text{C.}}{15^{\circ} \text{C.}}$. This oil retained its original character for more than a year, but in the ensuing six months a slight separation of concrete substance took place at the bottom of the flask.

(a) The fresh seed, (b) the ether extracted oil, and (c) the residue after extraction were submitted to examination.

(a) Action of the fresh seed.

On man. Obs. 1. Three hours after breakfast 9 grm. of the seeds of *O. triandra* was thoroughly chewed and swallowed, the mouth being rinsed with 20 c.c. of water, which was thereafter swallowed.

5 hrs. Borborygmi with occasional tendency to evacuation. Diuresis.

7 hrs. 30 mins. Strong prompting to evacuation, one action. Dejecta unformed.

20 hrs. Morning evacuation very soft, in part unformed.

25 hrs. Another evacuation of similar character.

On the succeeding morning there was still some looseness in the dejecta. There was neither griping nor discomfort during the observation.

Obs. 2. Two seeds of *O. triandra* were freed of integuments of the endosperm.

6 grms. were weighed, thoroughly chewed to a pulpy mass, and swallowed, the mouth being thereafter thoroughly rinsed with water, which was swallowed. No peculiar sensation in the pharyngeal region nor abdominal discomfort followed. In 7 hours' time there was some prompting to evacuation but it was not until 5 a.m. (12 hours after ingestion of the seed) that an action took place, preceded by a sensation of increased peristalsis and the occurrence of borborygmi. The dejecta were formed. A second evacuation occurred 4 hours later, whilst during the afternoon and evening "a distinct tendency to evacuation" was

thrice recorded. On the second day at 45 and 49 hours respectively after ingestion, soft evacuations. There was no discomfort or nausea throughout the observation.

Obs. 3. 3.3 grms. of the kernel of a fresh seed was thoroughly chewed; it was somewhat leathery and 4 minutes were required for its reduction to a fine pulp. Water afterwards.

4 hrs. 10 mins. No griping or discomfort but a distinct tendency to evacuation.

4 hrs. 40 mins. Tendency persists. Dejecta formed but soft.

6 hrs. 30 mins. Borborygmi. No griping.

15 hrs. Morning evacuation soft but formed.

20 hrs. Decided tendency to evacuation. Dejecta pale and only partly formed.

On the second day a slight laxative effect was still present.

These observations show in each case a laxative action, but they have been selected from many others in order to demonstrate the average effect of the doses indicated. Sometimes seeds were met with which had less activity than was to be anticipated from their weight. These probably contained less than the usual percentage of oil. An average dose of the fresh seed for an adult is from 4 to 5 gm.

On rabbits. This seed did not seem to be attractive to rabbits, consequently the feeding experiments were not of a satisfactory character.

On frogs. The introduction of the finely reduced seed with mucilage into the stomach or dorsal lymph sacs of decerebrated frogs was never followed by purgation and produced neither irritation, hæmorrhage nor toxic effect of any sort.

(b) *Action of the oil of O. triandra.*

On man. No nausea nor local irritant action was induced by ingestion of the oil. There was however a distinct laxative effect apparently identical with that produced by the fresh seed. No drastic effect was recorded from doses up to 4 c.c. Some diuresis was present, but there was no vesical irritation. A slight laxative effect usually, though not quite invariably, followed a dose of $\frac{1}{2}$ c.c., a soft evacuation resulting on the succeeding morning.

The effective dosage appears to be from 2 to 3 c.c. of the oil.

On rabbits. From healthy rabbits receiving a dietary of fresh vegetables, corn, bran and water the urine and fæces were collected for several days, special cages of large size adapted to the purpose being employed.

The results being sufficiently uniform the collection was continued for a further period of three days. On the morning of the fourth day a measured amount of the oil was dropped on to the back of the tongue of the animal and readily swallowed. Food was administered immediately afterwards to ensure the whole of the oil being transferred to the

stomach. No check in growth, no reduction of appetite nor interference in any respect with the health resulted from the administration of the oil. Though rabbits are by no means susceptible towards the purgative oils, perhaps from the feeble muscular development of the intestinal walls, a positive result was regularly produced from the administration of that of *O. triandra*. The doses required are however largely in excess of those which are active towards man, relative body-weight being considered. A feature of the action of *Omphalea triandra* oil (which is in accord with the effect upon man) is the long continuance of the laxative influence, the maximal increase of solid dejecta being usually recorded on the day succeeding administration rather than on the identical day.

Obs. 1. Rabbit (1850 grms.). Dietary 150 grms. corn and bran mixed with 100 c.c. water, together with 100 grms. fresh vegetables.

Amount of fæces and urine for three (control) days before administration of 1 c.c. oil of *Omphalea triandra*, and for three subsequent days.

	Fæces	Urine	
Day 1	65 grms.	95 c.c.	
2	80	75	
3	85	135	Daily average :—fæces 83 grms., urine 102 c.c.
4	87	163	1 c.c. of oil administered early on 4th day.
5	110	80	
6	91	137	Daily average :—fæces 96 grms., urine 127 c.c.

Obs. 2. Rabbit (2105 grms.). Dietary as above but 200 c.c. water.

	Fæces	Urine	
Day 1	60 grms.	185 c.c.	
2	75	225	
3	72	265	Daily average :—fæces 69.9, urine 235 c.c.
4	82	285	75 c.c. of oil administered early on 4th day.
5	87	257	
6	70	240	Daily average :—fæces 80 grms., urine 261 c.c.

These estimations show increase of fæces mainly on the second and of urine on the first day after administration of the oil. Some softening occurred in the constitution of the fæces in obs. 1. In both observations the specific gravity of the urine was reduced during diuresis, but excepting for its somewhat paler colour there was no material alteration in the secretion. The augmentation of urine was by 24% when the larger dose of oil was given with a smaller supply of water than it was when the initial secretion being very free under a doubled water supply, a smaller dose of oil was taken. In obs. 2 the increase is only of 11%.

Experiments of the same nature as those already described in

connection with the action of *Garcia nutans* were repeated with the oil of *O. triandra*.

This oil, as has been already shown, is but slow relatively in producing its action, so that in the course of prolonged observation only a slight tendency to increased activity of the circular musculature of the intestine was anticipated or, as matter of fact, observed. That the action is primarily local, that it is unattended by the irritant effect (seen in *garcia* seed administration), that it does not occur in the main intestinal track when the oil is introduced into an isolated loop of intestine, or vice versa, and that it is not occasioned at all by hypodermic injections, were the chief points elicited. Vagus stimulation, in conditions of hunger or satiety, after introduction of the oil into the intestine seem to favour an increased peristalsis, but this effect was not conspicuous.

On frogs. Injection of the oil of *O. triandra* whether into stomach or lymph sac was neither purgative, irritant, nor toxic. Normal frogs which received as much as $\frac{1}{15}$ c.c. in the dorsal sac showed no symptom whatever during the six weeks in which they were under observation.

(c) *Powder of the seed after extraction by ether.*

This powder was found to be quite inert when administered to man, rabbits or frogs.

OMPHALEA DIANDRA (MEGACARPA).

This seed is of large size flattened on dorsal and ventral surfaces; viewed from above is almost circular in outline. Its colour is dull grey (exceptionally rusty) and the thin, hard but brittle testa shows fine tuberculations on its surface arranged in a linear manner (Fig. 1, C). The ventral surface has two facettes separated by an obtuse median ridge. There is a small projecting beak at the micropyle. The seed floats. Measurement and weight. (Eight seeds examined.) Average length 33.93 mm. (largest 38 mm., smallest 30.5). Average width 31.43 mm. (largest 35 mm., smallest 28). Average thickness 21.62 mm. (largest 25 mm., smallest 18.5). The variation in length and width, respectively, are almost equal. Average weight (seed intact) 12.475 grms., the heaviest of the group being 15.84 grms., the lightest 7.6 or less than half the former.

Deprived of the testa and the thin silvery tegmen, the average weight of the seed was 9.225, the integuments therefore weighed 3.25 grms. The endosperm is flexible and easily reduced, white to creamy yellow in colour, embryo upright, cotyledons broad, albumen abundant. The taste is nutty and agreeable, sensation on chewing oleagenous. These seeds lost weight and decayed much more rapidly than those of *O. triandra*.

Of the seeds deprived of their coverings, 45 grms. were finely reduced in the mortar and thoroughly extracted with ether, which was thereafter evaporated at a gentle heat. The total oil obtained weighed 28.82 grms.,

representing a percentage of 47·33 for the seed intact or 64 % for the seed minus integuments.

The oil of *O. diandra* is of a pale yellow tint, slightly darker than that of *O. triandra*, it is limpid and has an oleagenous (in no way distinctive) odour and a bland nutty taste. Its specific gravity is 0·922 at 15° C. $\frac{15^\circ \text{C.}}{15^\circ \text{C.}}$, thus differing but slightly from the oil of *O. triandra*, in the third place of decimals. Both seed and extracted oil readily emulsify with mucilage.

The powder left after ether extraction is of a light greyish colour and is free from greasiness.

Note. Professor Dunstan has just forwarded me (Jan. 1908) the results of the examination of this oil, kindly permitting me to insert them in this paper. They are therefore appended. They embody many important additional data.

A small quantity of the seeds of *Omphalea megacarpa* (*Omphalea diandra*), which was forwarded to the Imperial Institute from the Botanical Department, Trinidad, has been examined in the Scientific and Technical Department of the Imperial Institute with the following results:

The seeds consisted of shell 28 % and kernel 72 %. The kernels, when extracted with light petroleum, yielded 65 % of oil (equivalent to 46·8 % of the whole seed). The oil was pale yellow, faintly bitter, readily soluble in chloroform or ether and soluble in 97 % alcohol to the extent of one part in 140 parts at 25° C. It burns without smoke or smell, and when exposed to the air in a warm place for several days it only becomes slightly thicker. The oil was slowly saponified by alkali with the formation of a white soap.

The following constants were determined:

Specific gravity	$\frac{15\cdot5^\circ \text{C.}}{15\cdot5^\circ \text{C.}}$	0·922
Acid value	1·47
Acid value calculated as oleic acid	0·77 %
Saponification value	190·3
Ester value	188·8
Iodine value	119·7
Melting point of fatty acids	36—37·5° C.
Solidifying point of fatty acids	31·5° C.

The oil is less viscous than castor oil and varies greatly in other respects, as is evident from the following comparison.

In particular, the iodine value of the *omphalea* oil is considerably

higher than that of castor oil, and indicates the presence of a larger proportion of unsaturated fatty acids.

	Omphalea Megacarpa Oil	Castor oil
Specific gravity $\frac{15.5^{\circ} \text{C.}}{15.5^{\circ} \text{C.}}$	0.922	0.960—0.968
Saponification value	190.3	176—183
Iodine value	119.7	83.4—85.9

(The close approximation in the percentages of oil obtained from the seeds sent to the Imperial Institute and to Aberdeen respectively, indicates that the samples were equally fresh, as otherwise the loss of weight which the seeds undergo upon keeping would cause a material alteration in proportion. It may therefore be inferred that the seeds of the two samples were similar.)

(a) The fresh seed, (b) the oil obtained by extraction with ether, and (c) the residue after extraction were used experimentally.

(a) *Action of the fresh seed.*

On man. In his letter accompanying the sample Mr Hart informed me that the seeds were occasionally used in Trinidad on account of their laxative action; about half a fresh seed to a dose.

Obs. 1. One kernel weighing 9 grm. was thoroughly chewed and swallowed, the fragments remaining in the mouth being washed down with 20 c.c. of water after rinsing.

5 hrs. later there was a distinct tendency to evacuation unattended by griping or discomfort of any kind. Dejecta formed but soft.

13 hrs. 30 mins. A full action of similar character. Diuresis.

16 hrs. After feeling of increased peristalsis, a diarrhoeic evacuation.

40 hrs. No renewal of purgation but the usual evacuation only partly formed.

Obs. 2. Of fresh kernel 6 grms. were taken.

5 hrs. 30 mins. and onwards. Slight tendency to evacuation, borborygmi occasional.

8 hrs. 30 mins. One rather soft evacuation.

23 hrs. The customary evacuation formed but soft.

47 hrs. Still somewhat soft.

Doses of 3—4 grms. were followed by a soft evacuation at the accustomed time on the following morning. Exceptionally from the larger amount an independent action followed in 7—8 hours.

(b) *Action of oil of O. diandra.*

On man. The action of the oil is closely similar to that of the fresh seed taken in proportion to its oily contents. It has been mentioned that the kernel yields 64 % of the oil so that a dose of 6 grms. of the former (which has been shown to be distinctly laxative) would furnish 3.8 grms. of the latter. From this amount of oil a fairly parallel action results, though

if anything the effect is slightly below that of 6 grms. of fresh seed in activity. This may be due to the fresh seed containing less than the usual percentage of oil, and also, to the probability that small but irregular fragments may cause an additional mechanical effect favourable to peristalsis, when the seed has been chewed and swallowed. The oil of *O. diandra* is so similar in character as well as in activity to that of *O. triandra* that there is a presumption of their identity. This point is not however definitely decided.

On rabbits. Feeding experiments were conducted in a similar manner to those in which the oil of *O. triandra* was employed.

Obs. 1. Rabbit of 1762 grms. Dietary 150 grms. corn and bran mixed with 100 c.c. water, and 100 grms. fresh vegetables. Amount of fæces and urine for three (control) days, before administration, and for the three days subsequent to administration of 1 c.c. oil of *Omphalea diandra*.

	Fæces	Urine	
Day 1	69 grms.	98 c.c.	
2	70	76	
3	75	110	Daily average :—fæces 71 grms., urine 95 c.c.
4	79	146	1 c.c. of oil administered early on 4th day.
5	92	92	
6	77	101	Daily average :—fæces 82·5 grms., urine 113 c.c.

Obs. 2. Rabbit of 2120 grms. Dietary as before but water only one half (50 c.c.).

	Fæces	Urine	
Day 1	71 grms.	60 c.c.	
2	62	85	
3	69	73	Daily average :—fæces 68 grms., urine 73 c.c.
4	84	100	·75 c.c. of oil administered early on 4th day.
5	67	95	
6	74	63	Daily average :—fæces 75 grms., urine 86 c.c.

In observation 1 the fæces are increased by 15 the urine by 18 % whilst in observation 2 the corresponding increase is by 11·2 and 11·8 %. Doses of ·6 c.c. and ·5 c.c. caused a slight laxative action, whilst ·4 and ·3 c.c. yielded results which were practically negative on four occasions, on a fifth however the larger dose was slightly though distinctly operative.

Diuresis after *O. diandra* was accompanied by a fall in the specific gravity of the secretion but by no other material alteration.

The action of the oil of *Omphalea diandra* (*megacarpa*) is laxative or purgative according to dose, it causes neither discomfort nor loss of appetite when given in the amounts specified to man or rabbit. There is no evidence that it acts as an hepatic stimulant. Its action is only moderately rapid after such administrations as have been recorded but

it is so far prolonged that the dejecta are usually distinctly soft in consistency 36 (or even 40) hours after a medium dose (man), whilst in rabbits the maximal effect is usually attained on the day after ingestion rather than on the same day. To this statement the result recorded in observation 2 is an exception. Slight diuresis occurs in man, unaccompanied by subjective symptoms. Diuresis in the rabbit is greatest on the day of administration.

The relatively slow development of action of the oil renders other experiments than those by feeding of small value. In so far as they have been employed the results are practically the same as for the oil of *O. triandra* (*q.v.*).

On frogs. Administration by the stomach or by injection into the lymph sac of frogs (amounts of oil ranging from $\frac{1}{20}$ to $\frac{1}{8}$ c.c. being employed) were devoid of result of any kind. Frogs in which the brain was undestroyed remained for the five weeks they were under observation in a perfectly normal condition after $\frac{1}{8}$ c.c. had been injected into the dorsal lymph sac.

(c) *Residue of ether extracted seed of O. diandra.*

Dietetic administration of the residue to man and to rabbits alike does not produce any noticeable effect.

SUMMARY.

1. The seeds of *Garcia nutans*, *Omphalea triandra* and *Omphalea diandra* (megacarpa) are possessed of purgative properties.

2. The action of the *Omphaleas* (apart from mechanical effect) appears to be entirely due to the presence of a fixed oil which though purgative, is bland and unirritating when given in effective doses. The degree of action of the fresh seeds stands in direct relationship to their oily contents.

3. The oils of the *Omphaleas* show little tendency to vary with time from their original condition and activity.

4. *Garcia nutans* seed, whilst containing a purgative oil, possesses an action in excess of the oily contents. It is probable that another (possibly deleterious) principle is contained in the seed, which may belong to the group of toxalbumoses.

5. The oil rapidly undergoes changes in condition and likewise in its activity.

6. *Garcia nutans* (probably also the two *Omphalea* seeds) increase peristalsis by stimulating the intramural nervous plexuses (Auerbach's, Meissner's) of the intestine. The intestinal juice is markedly increased by the first, probably by the others to a much slighter extent. The dose of the oils (as oils) of the *Omphaleas* is sufficient to produce a feeble mechanical action, contributory to the purgative effect which is proper to these oils.

All three seeds produce diuresis, absorption of their principles being thereby indicated. *Garcia nutans* is the most active in this respect, the *Omphaleas* are less so. This action is not exerted through the blood pressure, as the *Omphaleas* do not affect it and *Garcia nutans* causes no elevation but the reverse after it has acted for some time; it is presumable that the tissue of the kidney is directly stimulated, but the exact seat of action is undetermined.

7. As effective non-irritant cathartics the seed of *O. triandra* and *O. diandra* or their expressed oils would constitute valuable medicinal agencies. The dose sufficient to prove effective is small (relatively to castor oil) in bulk, and the taste is far from unpleasant.

Garcia nutans seed causes a prompt effect of a drastic character when given in large dose, but a simple purgative or laxative effect may be developed by modifying the dosage. The oil may probably be found the better and safer agent in the latter capacities. That it never produced a drastic effect may be due to the restricted dose in which it was given. It is obviously important that if an irritant hæmolytic principle is present in the seed, the preparation of the oil should be so conducted as to guarantee its exclusion.

The first of these was the discovery of gold in California in 1848. This led to a great influx of people to the West, and the discovery of gold in Nevada in 1859 led to a similar influx. The discovery of gold in Colorado in 1858 and in Idaho in 1860 also led to a great influx of people to the West.

The second of these was the discovery of silver in Colorado in 1859. This led to a great influx of people to the West, and the discovery of silver in Idaho in 1860 also led to a similar influx. The discovery of silver in Nevada in 1861 and in Arizona in 1862 also led to a great influx of people to the West.

The third of these was the discovery of copper in Arizona in 1851. This led to a great influx of people to the West, and the discovery of copper in Nevada in 1859 also led to a similar influx. The discovery of copper in Colorado in 1860 and in Idaho in 1861 also led to a great influx of people to the West.

The fourth of these was the discovery of iron in Colorado in 1859. This led to a great influx of people to the West, and the discovery of iron in Idaho in 1860 also led to a similar influx. The discovery of iron in Nevada in 1861 and in Arizona in 1862 also led to a great influx of people to the West.

The fifth of these was the discovery of lead in Colorado in 1859. This led to a great influx of people to the West, and the discovery of lead in Idaho in 1860 also led to a similar influx. The discovery of lead in Nevada in 1861 and in Arizona in 1862 also led to a great influx of people to the West.

The sixth of these was the discovery of zinc in Colorado in 1859. This led to a great influx of people to the West, and the discovery of zinc in Idaho in 1860 also led to a similar influx. The discovery of zinc in Nevada in 1861 and in Arizona in 1862 also led to a great influx of people to the West.

The seventh of these was the discovery of tin in Colorado in 1859. This led to a great influx of people to the West, and the discovery of tin in Idaho in 1860 also led to a similar influx. The discovery of tin in Nevada in 1861 and in Arizona in 1862 also led to a great influx of people to the West.

The eighth of these was the discovery of mercury in Colorado in 1859. This led to a great influx of people to the West, and the discovery of mercury in Idaho in 1860 also led to a similar influx. The discovery of mercury in Nevada in 1861 and in Arizona in 1862 also led to a great influx of people to the West.