

from 45 to 90 mgm. The *Ascarides* were expelled and their ova disappeared from the stools.

Clinical Trials.

With the assistance of Dr. A. K. Mukerji, assistant in the Hookworm Research Laboratory, we have tested the drug as an anthelmintic on a few cases infected with *Ascaris* and hookworm in the Carmichael Hospital for Tropical Diseases, and on a series of 18 cases infected with *Ascaris* in the Alipore Central Jail, Calcutta. We wish here to express our appreciation of the whole-hearted co-operation received from the Superintendent of the Jail, Lieut. H. A. Young, I.M.D.

The Indian santonin was accompanied in all cases by calomel and sodium bicarbonate. The amounts given and the details of preliminary and subsequent purges are given in the table.

All of the jail cases were kept on a liquid diet on the day that the drug was given. The stools from the hospital cases were saved and washed for 72 hours after the administration of the drug, those from the jail cases for 48 hours only. All of the patients' stools were re-examined for ova by the Kofoid and Barber technique 10 days later. As will be seen by reference to the table, the results compare very favourably with those ordinarily obtained with European santonin. Caius and Mhaskar (1923) gave 5 gr. doses of the latter to 19 men, curing 6 out of 9 who were given the drug in the morning, followed by a purge two hours later, and 8 out of 10 were given the drug in the evening followed by a purge next morning. Caius and Mhaskar obtained only 52.1 per cent. of cures with 48-minim doses of oil of chenopodium, but we have succeeded in curing 56.7 per cent. of 37 cases with 30 minims given in divided doses of 10 minims each at one hour intervals. Santonin is, therefore, more effective than chenopodium, though much more expensive.

Two of our hospital cases harboured hookworms as well as *Ascaris*; case No. 427 passed 15 *Ancylostoma duodenale*, but was subsequently still positive for hookworm; case No. 436 passed 11 *Ancylostoma duodenale*, but on subsequent treatment with carbon tetrachloride passed 178 *Ancylostoma duodenale* and 146 *Necator americanus*. The apparent differential effect on *Ancylostoma* is very interesting. Two other hookworm cases were treated with santonin but passed no hookworms, though both passed a few *Oxyuris*.

Conclusion.

Santonin extracted from *A. maritima* Linn (*A. brevifolia* Wall), which grows in the mountains of Kashmir (Baltistan), closely resembles in its physical, chemical and physiological properties the santonin imported from Europe. It satisfies all the tests laid down in the British and United States Pharmacopœias. Its therapeutic efficacy is just as good. The present market price of the Indian santonin is Rs. 670 per pound, but

if it is worked on a larger scale we have no doubt it could be considerably reduced.

We have much pleasure in expressing our indebtedness to Dr. A. K. Mukerji, Capt. P. De and Mr. N. R. Chatterjee for their help in this research. To Messrs. Smith, Stanistreet & Co. of Calcutta we are grateful for supplying Indian santonin, and to the Kashmir State Council, and especially to Mr. D. Nagerketti, Member in charge of Industry and Commerce, for supplying sufficient quantities of *A. maritima* Linn (*A. brevifolia* Wall).

REFERENCES.

1. Watts' "Dictionary of Economic Products in India."
2. "Pharmacographia Indica." Vol. II.
3. Viehoever and Capen. *American J. of Pharmaceutical Association*, May 1922, p. 393.
4. Greenish. "Eastern and Indian Drugs." 4, 1923, p. 225.
5. Greenish. *Pharmaceutical Journal and Pharmacist*, 1921, Vol. 10, 6, p. 2: 1922, Vol. 109, p. 85: 1923, Vol. 111, p. 94.
6. Caius, J. F. and Mhaskar, K. S. "Notes on *Ascaricides*." *Ind. J. Med. Res.*, Vol. XI, 1923, pp. 377-392.

A PRELIMINARY NOTE ON THE PHARMACOLOGICAL ACTION AND THERAPEUTIC PROPERTIES OF KUTH ROOT—*SAUSSUREA LAPPA*.

By R. N. CHOPRA, M.A., M.D. (Cantab.),

MAJOR, I.M.S.,

Professor of Pharmacology;

assisted by

CAPT. PREMANKUR DE, M.B.,

Assistant Professor of Pharmacology, School of Tropical Medicine, Calcutta.

(Indigenous Drug Series No. 4).

MANY species of *Saussurea* grow in the Himalayas at an altitude ranging from 2,000 feet to 13,000 feet above the sea level. The only species which has been used for its medicinal properties is *S. lappa* which grows in the North-Western portion of the Himalayas, especially on the moist slopes of the mountains round the valley of Kashmir. That is why among its various names one is *Kashmera* which means coming from Kashmir. The plant is well known both in the Ayurvedic and Tibbi medicine. It is called *kut*, *kot*, *kushi* (*costus*) or *patchak* in Hindi (Sanskrit—*Kushta* or *Kashmirja*) and *kust* in Arabic and Persian. For a long time a good deal of confusion existed as to which one of the large number of species of *costus* was used for its medicinal properties by the ancients, but Falconer has proved beyond doubt that the root of *Aucklandia costus*—now known as *Saussurea lappa*—was the species. The

plant grows as a very stout herb with large heart-shaped leaves, annual stem and thick perennial roots which are dug up in the months of September and October and are exported to Calcutta and Bombay in large quantities. From there the root is shipped to China and the Red Sea, and is used as a spice, as an incense and medicinally. So great is the demand that the Kashmere State authorities have started on a large scale nurseries and plantations of it under the Forest Department, and it is a great source of revenue to the State. The root has a peculiar aromatic fragrant smell which resembles that of orris root, and a bitter pungent taste. The uses of this root have been summarised by Baden Powell in his "Punjab Products" in the following terms:—

1. "Dried and powdered as the principal ingredient in an astringent stimulant ointment, applied to severe ulcerations.

2. Dried and powdered as a hair wash.

3. As a stimulant in cholera; an infusion made of cardamoms 1 dr., fresh kut 3 drs., water 4 ounces. One ounce every half hour. It is doubtless a powerful aromatic stimulant, and would be serviceable in any spasmodic disease.

4. It is universally employed by shawl merchants as a protector of Kashmere fabrics from the attacks of moth and other vermin.

5. The dried root is an agreeable fumigatory and yields excellent pastilles which burn fairly well.

6. It is exported in enormous quantities to China, where it is used as an incense. In every *hong* it is found; no mandarin will give audience until the *patchak* incense smokes before him; in every joss-house it smoulders before the Tribuda diety; in every floating junk in the Chinese rivers, —the only home of countless hordes,—Buddha's image is found, and the smoke of the *patchak* religiously mends its way heavenwards.....It is said to have the power of turning grey hair black. Carminative, stimulant, antiseptic, prophylactic, astringent, sedative, and insecticidal properties are referred to this remedy. "The Chinese apply it with musk to aching teeth."

The root is smoked in parts of India and in China as a substitute for opium.

Chemistry of *S. lappa*.

The drug was analysed by Schimmel and Co. (1892) who found that it contained 1.0 per cent. of essential oil with a strong fragrant and penetrating odour. Later, Semmler and Feldstein (Ber., 47,1914,2433,2687) made a thorough study of this oil. It has a specific gravity of 0.982, a rotatory power of 15° 20' in a 100 mm. tube. Its boiling point is 275° C. and above 315° C. the oil decomposes, giving a vapour with a very disagreeable odour. Little or no attention has been paid to the other constituents of the root, though mention has been made of the presence of small quantities of an alkaloid. Dr. Sudhamoy Ghosh in collaboration with Mr. Nihar Ranjan Chatter-

jee made a complete analysis of the dry root, which was kindly supplied by the Kashmere State authorities. They found that besides the essential oil, and the alkaloid, there was a body of glucosidal nature in fairly large quantities. The composition of the root according to this analysis is as follows:—

1. Essential oil .. 0.86 per cent.
2. Alkaloid .. 0.2 per cent.
3. Glucoside .. Exact proportions not yet determined.
4. Resins .. 8.3 per cent.

The details of this work will be published separately.

Pharmacological action of *S. lappa* (kuth).

We tested the action of the three active principles separately. On undifferentiated protoplasm the essential oil has a markedly toxic action, but the action of the alkaloid is not so pronounced, and the glucoside has little or no action at all in this direction. In concentrations of 1 in 2,000 the essential oil kills *Paramœcium caudatum* instantaneously; 1 in 5,000 solutions slow the movements rapidly, the paramœcia crawl along the bottom, move in circles and die in less than 5 minutes.

Even a dilution of 1 in 10,000 produces a definite effect; the movements of the ciliate become sluggish and some of them die in 10 minutes. The alkaloid in a concentration of 1 in 400 kills the paramœcia and 1 in 1,000 produce slowing and death in 10 minutes, but this was probably due to the acid reaction of the salt of the alkaloid and not to any inherent property of the alkaloid.

We also tried the bactericidal properties of these bodies on *staphylococcus albus* and *aureus streptococcus*, *B. coli* and *B. diphtheria*, and the results are given in the following table.

Bactericidal action of Kuth essential oil.

ORGANISM.	APPROXIMATE DILUTIONS.				
	1-2,000.	1-3,000.	1-4,000.	1-5,000.	1-10,000.
<i>Streptococcus pyogenes aureus</i>	+	+	±	±	±
<i>Staphylococcus aureus</i> and <i>albus</i>	+	+	±	±	±
<i>B. coli</i>	±	±	—	—	—
<i>B. diphtheria</i>	±	—	—	—	—

+ No growth : ± inhibition : — no effect on growth.

The alkaloid—except in concentrations of 1 in 500—produced very little effect. These experiments show the strong antiseptic and disinfectant properties of the essential oil against streptococci and staphylococci, and one can understand why the drug is used in the form of an ointment against boils, ulcers, wounds, etc.

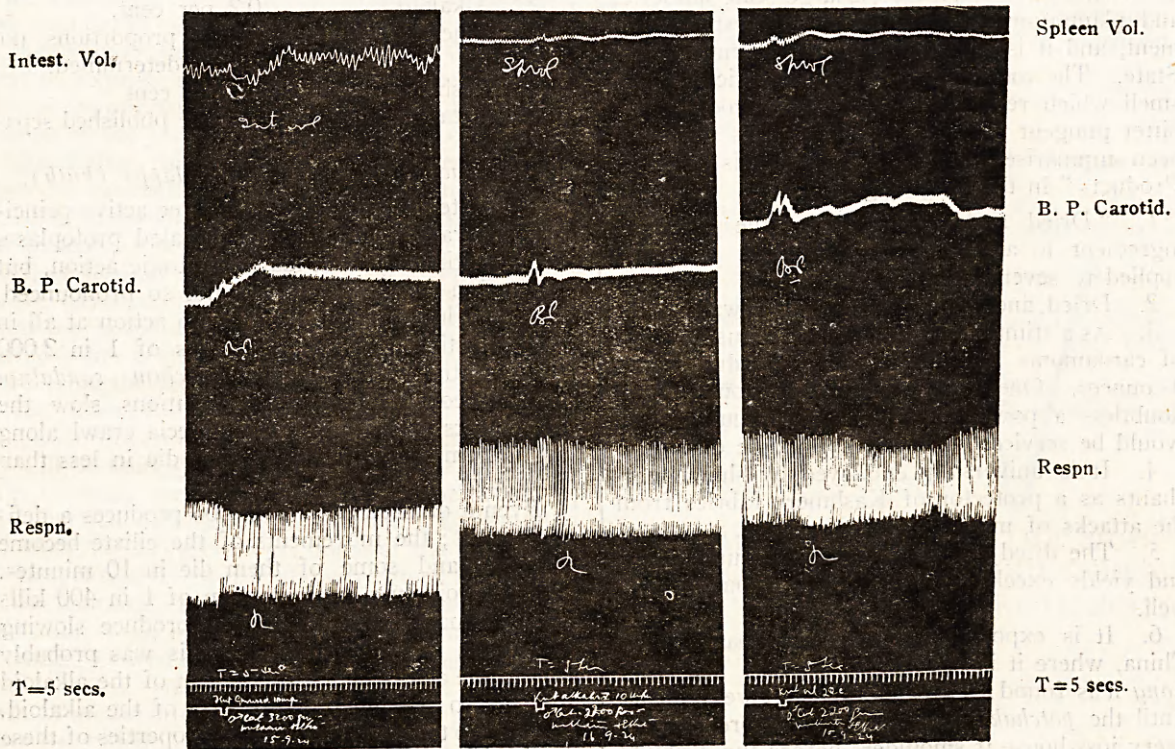
Externally.—The essential oil has a strong fragrant, aromatic smell. The odour is very penetrating and adheres for a long time to the

part on which it is applied. The Chinese use it largely as a scent. The oil is only slightly irritating, when applied to the skin and mucous membrane. Subcutaneous injections of this oil, as

well as those of the alkaloid and glucoside, produce no irritating effects.

Internally.—The extract made from the root has a pungent bitter taste in the mouth. In the

GRAPH I.

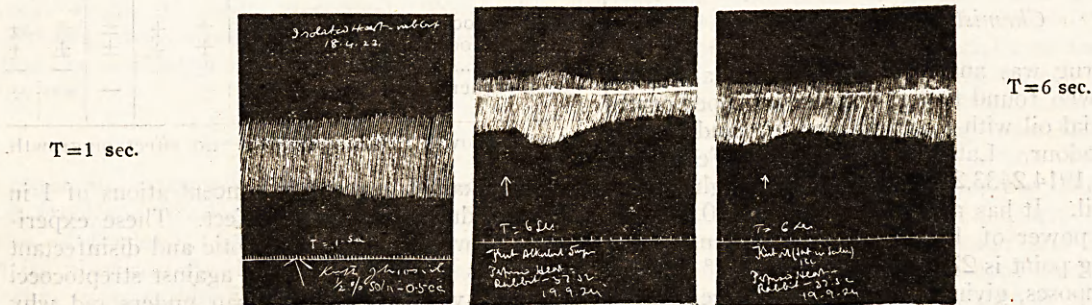


Kut Glucoside 10 mgm. male cat 3,200 gms. urethan and ether.

Kut Alkaloid 10 mgm. male cat 2,200 gms. urethan and ether.

Kut oil sat. saline soln. 2 c.c. male cat 2,200 gms. urethan and ether.

GRAPH II.



Kut Glucoside 1% soln. 0.5 c.c. Perfusion - isolated Heart-rabbit.

Kut Alkaloid 5 mgm. Perfusion - isolated Heart-rabbit.

Kut oil sat. saline soln. 1 c.c. Perfusion isolated Heart-rabbit.

stomach it gives rise to a feeling of warmth; the powdered root has a similar effect. After large doses, 10 to 20 c.c. of the extract (1 c.c. = 1 gm. of the root) the patients may complain of a feeling of discomfort in the abdomen, lasting for several hours, and sleepiness. No other untoward effects were noticed. The drug has mild carminative properties but does not produce any increase of intestinal peristalsis or purgation. On the isolated intestine of rabbits the effect of the essential oil in approximate dilutions of 1 in 120,000 to 1 in 60,000 is to inhibit the movements; the rhythm is interfered with and the peristaltic movements become irregular. The alkaloid produces an increase of tone and amplitude, the glucoside inhibits the movements without interfering with their rhythm. Intravenous injections of these active principles in small doses have no effect on the peristaltic movements. Intestinal volume, however, shows a definite increase, probably due to vaso-dilation (*see graph I*). The spleen and kidney volumes also show some increase, indicating that the effect probably involves the whole of the splenic area. Section of the vagi does not alter these effects in any way.

Circulatory System.—Intravenous injections of a saturated solution of the essential oil in saline (2 mgm.) cause a slight rise of blood pressure, which is not steady but often shows slight oscillations. The glucoside produces a small but persistent rise of blood pressure and a slight increase in the amplitude of the heart beats. This effect is very much more marked in some animals than in others. The alkaloid has hardly any action on the blood pressure. Section of the vagi produces no alteration in these effects. On the perfused isolated heart of the rabbit both the alkaloid and the glucoside have a stimulating effect, the amplitude being increased without alteration in the rhythm; there is some after-depression in the case of the alkaloid. Weak concentrations of the essential oil, i.e., approximately 1 in 10,000 to 1 in 15,000 are depressing, but the effect soon passes off. (*see graph II*).

From these experiments the use of this drug as a stimulant in diseases like cholera and typhus, where the circulatory system is much depressed, can be comprehended. The alkaloid and glucoside stimulate the heart directly and the essential oil probably acts reflexly, giving rise to pressor effects.

Respiratory System.—Both the essential oil and the glucoside given intravenously have a slight though a definite broncho-dilator action. This was much more marked as a rule in the dog, which is essentially a vagotonic animal, than in the cat, which is sympathetotonic. This effect disappears when the vagi are cut. It would appear therefore that the drug acts by inhibiting the increased tone of the vagus which occurs in a class of asthmatics and hence its reputation in the treatment of this disease. The alkaloid has no

action in this respect. Inhalation of the oil in animals under anaesthesia produces no effect on the bronchial musculature. The drug has a well marked expectorant action.

Genito-Urinary System.—The essential oil is partly excreted by the kidneys and we are enquiring into its antiseptic properties in the urine. The liquid extract given internally has a marked diuretic effect; in one of our cases, a boy aged 13 years, the quantity of urine rose from 20 to 70 ounces. The kidney volume is slightly increased, owing to vaso-dilation. None of the active principles have any noticeable effect on the isolated uterus of the rabbit or the guinea-pig.

Central Nervous System.—No effect is seen with ordinary therapeutic doses; larger doses of the extract produce giddiness, headache and sleepiness, due probably to depressing effect of the essential oil on the central nervous system. When smoked, the drug produces some stimulation which lasts a few minutes; soon the patient feels dizzy and sleepy and this depression lasts several hours. Larger amounts are said to produce narcosis like opium smoking.

Clinical Trials.—From the earliest ages, the drug has been used in India in a variety of conditions. In Ayurvedic medicine it is used as a tonic, and as an aphrodisiac and in diseases of the respiratory tract, especially asthma.

We are informed by Mahamohopadaya Kabiraj Gana Nath Sen, M.A., L.M.S., that it is extolled for the treatment of malaria in the Atherva-Veda. Tibbi writers recommended it against rheumatism, in persistent hiccough and as an anthelmintic. The therapeutic properties of the drug and the claims made regarding it are under investigation and will be published in detail later. More work is necessary before any definite conclusions can be arrived at. We will briefly refer however to the results obtained so far.

The drug is recommended in spasmodic conditions of the respiratory passages, especially when the bronchial musculature is contracted. The rationality of this view is borne out by our experiments on animals. A large class of asthmatics in India come under the category of vagotonics. In these patients the action of the vagus is increased, owing to certain causes, producing spasm of the bronchial musculature and vaso-dilation of the bronchial mucosa, which give rise to asthmatic attacks. These effects can be relieved by giving atropine, which diminishes the vagus action, or adrenalin, which stimulates the antagonistic action of the sympathetic. Both these drugs have obvious disadvantages. The *kuth* root appears to have a marked and lasting effect in decreasing vagal tone and at the same time relieves the congestion of the bronchial mucosa by its expectorant action, which, at any rate, is absent in the case of atropine. So far it has proved to be a very useful drug in these cases. We have tried the alcoholic extract in a series of cases of asthma

and found that it not only had a remarkable effect in relieving the spasms, but it also prevented recurrence of attacks, loosened the phlegm and cleared the respiratory passages. A patient in the hospital who was so bad that he could not sleep at night without an injection of adrenalin, when put on 2 to 4 drms. of the extract three times a day, had no recurrence of attacks while the drug was being administered. All our asthmatic patients benefited under this treatment. In one case of persistent hiccough in which we tried the extract, the patient was markedly relieved. In Tibbi medicine it is recommended for rheumatism and much stress is laid on its anthelmintic properties. In collaboration with Drs. McVail and A. K. Mookerjee of the Hookworm Research, the drug was tried in the Carmichael Hospital for Tropical Diseases on cases of hookworm, *Ascaris*, *Trichuris* and *Tænia* infections. It was given in the form of powdered root, and as alcoholic extract; magnesium sulphate being given 2 to 3 hours afterwards. In some cases giddiness and headache occurred, but very few worms were expelled. As an anthelmintic the drug is of little value. This was borne out by our experiments with some of these entozoa *in vitro*; the parasites kept alive and active for hours in very concentrated solutions of the active principles. Dr. Muir, in charge of the Leprosy Research, very kindly tried the powdered root and the essential oil locally in some cases of leprosy, but no benefit resulted.

Conclusions.

1. The active principles of *Saussurea lappa* are (a) an essential oil; (b) a glucoside; (c) an alkaloid.
2. The essential oil and the glucoside are pharmacologically active bodies. The alkaloid is less active.
3. The essential oil has strong antiseptic and disinfectant properties especially against the streptococcus and staphylococcus; the alkaloid and the glucoside have little or no effect in this direction.
4. The glucoside causes a small but a persistent rise of blood pressure; the essential oil does this to a lesser degree.
5. Both the glucoside and the essential oil have a slight but a definite broncho-dilatory effect. The alkaloid is inactive in this respect.
6. The powdered root and the alcoholic extract are expectorant and are beneficial in asthma. They cut down attacks and reduce their frequency.
7. The drug has no anthelmintic properties.

We have much pleasure in expressing our gratitude to Dr. Sudhamoy Ghosh, M.Sc. (Cal.), D.Sc. and Mr. Nihar Ranjan Chatterjee, M.Sc., who carried out the analysis of this root. This involved very hard work extending over a year, and the details will be published by them separately. To Dr. A. K. Mukerji, Assistant to the Hookworm Research Worker, we are grateful

for trying the drug in cases infected with intestinal parasites.

REFERENCES.

1. Watts' "Dictionary of Economic Products of India."
2. Pharmacographia Indica, Vols. II and III.
3. *Khazanat-el-adwia*. (A treasury of medicines) Publishers Newal Kishore Press, Lucknow.

SURGICAL, SUNDRIES.*

By C. A. GOURLAY, D.S.O., M.D.,

LIEUT.-COLONEL, I.M.S.,

Civil Surgeon, 24-Perganas.

ANÆSTHESIA.

THIS is a subject of importance, whether you are dealing with accidents or disease, with clean or septic cases. In my student days administration of an anæsthetic was practically synonymous with administration of chloroform.

At the present day our duty demands very much more than this and yet in India how often does one see a patient subjected to excruciating pain for want of any anæsthetic, making a noise which distracts the attention of surgeons and attendants, struggling in a way which makes accurate work impossible, and suffering an altogether unnecessary degree of shock. Or again, how often does one see a patient brought amongst total strangers, laid upon a table, a mask suddenly clapped over his mouth, a suffocating atmosphere created in which he strikes out or struggles in terror of his life, only to find himself set upon by able-bodied persons who hold his arms and legs down to the table. Put yourself in the place of either of these patients and try to think how you would like it. But the matter is not one of mere sentiment. In both these cases, the patient has been subjected to a quite unjustifiable degree of shock and not infrequently, the results of shock are, to say the least of it, very disconcerting.

I recollect, once, a case of a man with retention of urine on whom I proposed to pass a catheter. I found he had a very small meatus and I thought I could stretch it with one or two of the smaller bougies. I did so quite gently as I thought but without an anæsthetic. The man complained of considerable pain during the procedure. No further manipulation was necessary as he felt an inclination to pass urine voluntarily after a slight dilatation. Later, this man collapsed and in 24 hours he died of shock.

This is an extreme case, but I want to impress on you the very real danger of shock, and to bring

* Being a paper read before the Medical Section of the Asiatic Society of Bengal, on July the 9th, 1924.