

On December 16th another batch of 23 *A. stephensi* was fed on the same patient, the crescents being 160 per cubic millimetre. The mosquitoes were dissected as follows:—

The above notes we submit create a strong presumption that Atebrin administered to a patient suffering from malaria completely prevents the development in the mosquito of any

On	Number of <i>A. stephensi</i> dissected	Days after feeding	EXAMINATION OF	
			Stomachs	Salivary glands
7-1-32	2	22	<i>Nil.</i>	<i>Nil.</i>
8-1-32	5	23	<i>Nil.</i>	One mosquito showed very scanty infection.
9-1-32	5	24	One mosquito showed an oöcyst.	<i>Nil.</i>
11-1-32	5	26	Two showed oöcysts.	<i>Nil.</i>
16-1-32	6	31	One showed oöcysts.	The same mosquito showed scanty sporozoites.

Total percentage with development forms — $\frac{5}{23} = 22$ per cent.

On December 18th another batch of 9 *A. stephensi* were fed on the patient, who on the 19th had 120 crescents per cubic millimetre the result of the subsequent dissection being as follows:—

gametocyte from that human host, that considerable inhibition to development exists the day after the drug has been discontinued, and that the parasite resumes its developmental powers three days after the discontinuance.

6-1-32	4	19	Two mosquitoes showed oöcysts.	All showed scanty infection.
7-1-32	2	20	Two with oöcysts	Two with scanty infection.
19-1-32	3	32	One with oöcysts	All with scanty infection.

Total percentage with development forms—100 per cent.

ON THE FAILURE OF *TODDALIA ACULEATA* IN THE TREATMENT OF MALARIA

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Toddalia aculeata (Syn. *T. asiatica*, *T. rubi-caulis*, *T. nitida* and *Scopolia aculeata*) is a climbing shrub of natural order Rutacea. Vernacular, Sanskrit, *kanchana*; Hindi, *kanj*; *dahan lahan* (Rajputana); *meinkara* (Nepal); *saphijirik* (Lepcha); *melkaranai kandvi* (Tamil); *konda-kathinda* (Telegu); *jangli-kali-mirchi* (Bombay); *kudur-miris* (Ceylon).

It grows in sub-tropical climates of India, Java, Sumatra, China, etc. It is a large scandent shrub with branches covered with prickles, on broad corky cones; the leaflets are crenulate, varying in length from $1\frac{1}{2}$ to 4 inches, the flowers small, cream coloured in axillary panicles, longer than the petiole; the calyx is glandular, petals—five, imbricate, stamens—not exceeding five, ovary—five-celled, style—short, stigma—five-lobed, and ovules—two superposed in each cell. The root is woody and in cylindrical flexuose pieces, from $\frac{1}{2}$ to 2 inches in

diameter. The root bark is about $\frac{1}{12}$ of an inch thick and consists of a soft yellow corky external layer, wrinkled longitudinally, a thin yellow layer and a firm brown middle cortical layer.

Chemical composition

The bark contains a resin, an essential oil resembling oil of citron in flavour, and a bitter principle identical with berberine.

The present investigation was undertaken because of the alleged anti-malarial properties of its root bark in the indigenous system of medicine, and of the good results in malaria reported by earlier investigators. Rheede (Kirtikar and Basu, 1918), who gave an extensive trial to this drug, stated that as an anti-periodic and antipyretic, it was equal, if not superior, to quinine and other alkaloids of cinchona. In his experience, even in obstinate cases of malaria where quinine or arsenic had failed, favourable results followed the use of this drug. Dr. Bidie of Madras found it a valuable tonic in debility after malaria fever and in convalescence from exhausting diseases. This result was confirmed by Surgeon Major Kirtikar in cases of malaria cachexia. An infusion of the bark of this shrub was tried in several mild

cases of malarial fever in the out-patient department of the Madras General Hospital with very beneficial results. The object of the above investigation was to verify the conclusions of the previous investigators.

In the present investigation, root bark which was supplied to us by the Forest Economist, Dehra Dun, was used in the form of tincture, prepared according to the directions laid down in the Indian *addendum* to the British Pharmacopœia, in doses of $\frac{1}{2}$ -1 fluid drachm. No other drugs were administered whilst this tincture was being given except the ordinary purgatives.

The drug was first tried in the out-patient department of the King George's Hospital during the malarial season of 1930. The first report of the physician in charge was that the drug had some beneficial effect on cases of malaria, but after a few weeks further trial he was of opinion that the drug was not having any marked effect and that in most cases he had to fall back upon quinine or cinchona. The inconclusive reports from the out-patient department necessitated a trial in the wards, controlled by repeated blood examinations. The blood of cases in the wards which were put on this tincture was first examined for malarial parasites and only such cases as were positive were given this root bark. The results obtained with this series are given in table I. A glance at this table will show that 7 out of these 12 cases were not benefited by this treatment

(extending over 5 to 6 days) either as regards their clinical symptoms or the parasites. In cases 4 and 7, although the fever abated the parasites were still found in the blood. In cases 3, 8 and 9 two of which were of the mixed infection the benign tertian parasites disappeared, but the crescents remained unaffected. Fever abated in these three cases as well. Although these results were not encouraging yet in view of the fact that in a small proportion of the cases clinical symptoms were relieved, and in a few the parasites disappeared from the blood, it was thought desirable to give it a further trial. This was done during the months of August and September 1931 in the out-patient department.

In this series, such cases were selected which clinically appeared to be malarial fever (the criterion followed being intermittent fever ushered in with rigor and enlarged spleen). Blood films were also taken and the patient given toddalia mixture, three times a day (tincture toddaliæ 5i, magnesium sulphate 5i, aquam ad 5i).

Out of 24 cases of this series in only 10 were malarial parasites found (9 *P. vivax* and 1 *P. falciparum*), and none out of these 10 was benefited by toddalia mixture, given for 5 to 7 days. Every one of these cases was relieved with a few doses of cinchona mixture. In one case fever abated, but parasites were still detected in the blood. Of the remaining 14 cases, which clinically simulated malaria but in

TABLE I

A series of cases of malarial fever, treated in the Wards of King George's Hospital with tincture toddalia

Serial number	Name	Age	Sex	Blood findings before treatment	Date of commencing toddalia	Blood findings while on toddalia	Date of starting quinine	Blood findings whilst on quinine
1	Rani ..	50	F.	M. T. Rings ++ Crescents +	12-8-30	15-8-30 ++ 16-8-30 ++	17-8-30	19-8-30 (Neg.)
2	Ram Pyare ..	15	F.	B. T. Rings ++ Amœboids ++	11-8-30	14-8-30 ++ 15-8-30 ++	16-8-30	20-8-30 (Neg.)
3	Mrs. T. J. ..	30	F.	B. T. Rings ++ Crescents +	6-8-30	10-8-30 11-8-30 Crescents ++	Temperature normal from the 7th.	
4	Ganga Deen ..	35	F.	Crescents +	12-8-30	16-8-30 Crescents +	Temperature normal since the 13th.	
5	Usman ..	25	M.	B. T. Rings ++	16-8-30	19-8-30 +++	20-8-30	22-8-30 (Neg.)
6	Mr. K. ..	20	M.	B. T. Amœboids +++	17-8-30	20-8-30 ++	20-8-30	22-8-30 (Neg.)
7	Hanuman ..	14	M.	B. T. Rings ++	8-8-30	12-8-30 ++ 14-8-30 ++	Temperature normal since the 10th.	
8	Phoolchand ..	25	M.	B. T. Rings + Crescents ++	20-8-30	25-8-30 26-8-30 Crescents +	Temperature normal from the 22nd.	
9	Panday ..	30	M.	B. T. Amœboids ++	22-8-30	27-8-30 Neg.	Temperature normal from 25th.	
10	Shafat Ahmad ..	20	M.	B. T. Amœboids ++	18-8-31	22-8-31 ++	23-8-31	25-8-31 (Neg.)
11	Imdad Husain ..	50	M.	B. T. Rings ++	18-8-31	22-8-31 ++	25-8-31	27-8-31 (Neg.)
12	Zahir Ali ..	18	M.	B. T. Rings ++	20-8-31	23-8-31 +	24-8-31	27-8-31 (Neg.)

TABLE II

Statement showing action of infusion toddalia and infusion cinchona bark on paramœcia

	Strength	EFFECT ON PARAMœCIA			
		10 minutes	½ hour	1½ hours	3 hours
Infusion of <i>Toddalia aculeata</i> ..	1 in 10	No effect	No effect	Some dead	All dead
	1 in 50	Do.	Do.	No effect	No effect
	1 in 100	Do.	Do.	Do.	Do.
Infusion cinchona	1 in 10	Sluggish	All dead
	1 in 50	No effect	Sluggish	All dead
	1 in 100	Do.	No effect	No effect	No effect

which no parasites were detected in the films examined in the pathology department, 10 got relief with this tincture in 2 to 5 days, and 4 remained unaffected during the first week and then stopped attending the hospital. It is possible that some of these 14 were cases of mild type of malarial infection in which the parasites were too few in the blood to be detected on routine examination, but it is equally possible that in these cases the enlarged spleen was due to a previous infection and that their present fever was due to causes other than malaria. We are inclined to take the latter view particularly for purposes of an investigation of this nature which aims at getting some definite results. Thus out of 26 cases of proved malaria, the parasites persisted in the blood with this treatment in 23 cases and the symptoms remained unabated in 20 cases. Beneficial results were obtained in only a small proportion of the cases (3 out of 26) which is often the case even when no treatment is given.

An attempt was also made to find out if the drug had any toxic effect on unicellular organisms such as paramœcia. A freshly-prepared infusion was used and comparison was obtained with a similarly-prepared infusion of cinchona bark. The results obtained are given in table II from which it is apparent that its toxic effects are very feeble, being only about one fifth that of cinchona.

Conclusions

1. In our series of cases of malarial fever caused by *P. vivax* and *P. falciparum*, tincture toddaliæ, prepared from the root bark, had no marked effect on the parasites in the blood or on the temperature.
2. Its toxic effects on paramœcia are very feeble compared to that of cinchona.
3. Evidence is thus brought to show that the drug is useless in the treatment of malaria.

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BERBERINE AND BERBERINE-CONTAINING PLANTS IN PHARMACOLOGY AND THERAPEUTICS

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BERBERINE-CONTAINING plants have been used by both the Hindu and Mohammedan physicians as stomachic and bitter tonic in the same way as quassia and calumba. They have also been used as antiperiodics and alteratives in remittent types of fevers. The root paste is used as a paint for acute ophthalmia in children. In the treatment of leprosy, snake bite, jaundice and vomiting of pregnancy, berberine-containing plants have been largely used. The fruit or berries of *B. asiatica* are given as a cooling laxative in children, the stems are said to be diaphoretic and laxative, and are recommended in rheumatism. The root-bark is rich in bitter principles and is used as a tonic and anti-periodic. Instead of the root-bark, the root itself was employed as an anti-periodic, diaphoretic and anti-pyretic, and its action was believed to be as powerful as quinine. A decoction made from the root was said to be an excellent remedy against malaria. The dried extract made from the root known as *rasaut* or *ras* is used as a purgative for children, as a blood-purifier and as an external application in conjunctivitis in combination with alum, or alum and opium. It is used as a local application for indolent ulcers. It has also been used for gastric and duodenal ulcers by the indigenous practitioners.

The alkaloid berberine has been used by physicians practising the western system against