

## **Iboga Alkaloids**

The bark of the root of *Tabernanthe iboga* contains about 12 alkaloids (Downing, 1962). Of these the best known is ibogaine, a tryptamine derivative. This plant, named in 1889 by Baillon, was used by the natives of West Africa and the Congo to increase resistance against fatigue and tiredness and as an aphrodisiac. Dybowski and Landrin (1901) extracted the psychologically active alkaloid which they named ibogaine. They reported that the natives considered the plant equivalent or similar to alcohol, that it was a stimulant which did not disturb the thought processes of the user.

They wrote "l'Iboga avait sur eux une action identique a celle de l'alcool sans troubler la raison." Turner *et al.* (1955) believed this was a denial by the natives that ibogaine was psychotomimetic. But this is an interpretation based upon the belief that humans having perceptual changes must have some disorder of thought. Many unsophisticated subjects taking LSD, mescaline, or psilocybin do have changes in thought but after they became experienced with these compounds, changes in thought are rare. Native consumers of peyote, the *Psilocybe* mushrooms and, perhaps, iboga extract, can have vivid perceptual changes with no disturbance in thought.

According to Landrin (1905), Guien described the effect of chewing large quantities of roots on natives being initiated. They became very tense, developed an epilepticlike state during which they became unconscious and uttered words considered prophetic. An initiate would have a set toward initiation which combined with the iboga root could well produce these extreme states of excitement.

Dybowski and Landrin (1901) found ibogaine was as active psychologically as the whole root. Small doses produced states of excitation while massive doses were narcotic which they compared to massive quantities of alcohol. Haller and Heckel (1901) also extracted an alkaloid, probably the same one, which they called ibogaine.

Pouchet and Chevalier (1905) found that ibogaine given intravenously to dogs produced violent excitation motor incoordination, hallucinations, paraplegia, paralysis, and anesthesia. Tetanic convulsions occurred just before death. Death came from respiratory arrest and the heart stopped in diastole. They concluded ibogaine was a stimulant of the central nervous system. They found it was also a good surface anesthetic less intense than cocaine. There was a period of hyperesthesia before the anesthesia came on.

### **ANIMAL BEHAVIOR**

According to Lambert and Heckel (1901) subconvulsive doses produced marked changes in dogs. They developed a state of excitation and appeared to have hallucinations. The dogs crouched in a corner, growled and barked. After 1 hour they were normal. Phisalix (1901) gave dogs ibogaine by vein. A mild cerebral excitation was produced by 0.75 mg/kg. The dogs were more active and responded with alacrity to caressing. When 1 mg/kg was given,

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the dogs suffered incoordination and hallucinations. Ibogaine also produced excitation in other animals.

Lambert (1902) found ibogaine had a markedly cumulative effect in frogs. When 5 mg was injected, there was no noticeable effect, but the same dose given on succeeding days produced an increase in response, of the kind seen with higher initial doses. After several days the dose was toxic for some frogs. The toxic dose for frogs for one injection was 500 mg/kg. This suggests a different mode of activity for ibogaine than for LSD where toxicity does not accumulate.

Schneider and Sigg (1957) corroborated the findings of the early French scientists. They gave 2-10 mg/kg by vein to cats and dogs. In cats the effect came on immediately. They became very excited, began to develop a tremor, and developed rage reactions. The animals remained in one place, while hissing as if trying to frighten away an imaginary object. Often they tried to hide in a corner or to climb over the walls. At the height of the excitatory phase the animals had peculiar clinic extension of all the limbs which spread the limbs in all directions with the abdomen on the floor. The cats frequently mewed. Maximum excitement was reached in 10-20 minutes. Usually there were marked autonomic reactions including pupillary dilatation, salivation, partial piloerection, and tremor. After 1-2 the cats were normal.

Gershon and Lang (1962) also saw the marked excitatory properties of ibogaine. Dogs became more anxious and alert and did not recognize their regular handlers. Body tremor and shaking was noted in dogs and also in sheep. In dogs ibogaine caused a peculiar stance with legs apart and back arched.

In anesthetized dogs, cats, and sheep, ibogaine was analeptic and anesthesia was lightened.

Gershon and Lang (1962) and Schneider and Rinehart (1957) found that pretreatment with atropine prevented the rise in blood pressure produced in conscious dogs by ibogaine but according to the former the behavioral changes were not affected. Schneider and Rinehart (1957) suggested the increase in blood pressure produced by ibogaine was due to its stimulating effect on the reticular activating system. Anesthetized dogs, unable to respond to stimulation, suffered a decrease in blood pressure.

#### CHEMISTRY

Ibogaine had long been considered an indole because it reacted in color tests as an indole.

[ ... chemical structure is here in text ... ]

Another similar alkaloid voacangine present in *T. iboga* was first isolated from *Voacanga africana*. Renner et al. (1959) isolated 1 known and 4 new alkaloids from *C. durissima* Stapf, Isovoacangine (first found in *Stemmadenia* species by Walls et al., 1958). The new compounds were conopharyngine, conodurine, conoduramine, and alkaloid E. Some alkaloids from *iboga* are tabulated below.

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Alkaloid	R1	R2	R3
Ibogaine	OCH3	H	H
Ibogamine	H	H	H
Tabernanthine	H	OCH3	H
Coronaridine	H	H	COOCH3
Voacangine	OCH3	H	COOCH3
Isovoacangine	H	OCH3	COOCH3
Conopharyngine	OCH3	OCH3	COOCH3

## PHARMACOLOGY

Lambert and Heckel (1901), Phisalix (1901), Lambers (1902), Raymond-Hamet (1941a,b), Raymond-Hamet and Rothlin (1939), and Rothlin and Raymond-Hamet (1938) completed the early studies on the pharmacology of ibogaine.

When injected subcutaneously into the frog, voluntary movements and reflex activity were abolished, but muscles were still excitable. Respiratory movements were reduced for a time, but there was no effect on the heart rate. The toxic dose was about 0.5 gm/kg. In the guinea pig, rabbit, and dog, death occurred during convulsions.

In dogs, respiration was accelerated, the temperature became elevated, and the pupils became widely dilated and unresponsive to light.

Lambert and Heckel reported that sublethal doses produced an anesthetic effect around the area of the injection. They compared the surface anesthetic properties of ibogaine with cocaine. A few drops instilled in the eye abolished corneal sensation, although the solution produced a slightly caustic sensation in the eye.

Ibogaine inhibited contraction of the small intestine of the rabbit and the large intestine of the guinea pig. It decreased the inhibitor action of adrenaline but did not alter the effect of acetylcholine. Ergotamine reversed ibogaine's action. Ibogaine had no direct effect on the seminal vesicle of guinea pig but inhibited almost completely the motor effects of adrenaline and acetylcholine, that is, it antagonized adrenaline, acetylcholine, yohimbine, and atropine.

Schneider and Sigg (1957) studied the effect of ibogaine on the electroencephalogram of cats. Cats with cerveau isole and encephale isole preparations as well as curarized animals showed a typical arousal syndrome when a 2-5 mg/kg were given by vein. A slow frequency high-amplitude pattern was altered to a pattern of fast low-amplitude activity. It resembled the change during direct stimulation of the reticular formation. After 1/2-1 hour the patterns were normal. Pretreatment with atropine (2 mg/kg) blocked the arousal effect of ibogaine.

There were only slight changes in reflexes. The knee jerk reflex was reduced slightly. There was no effect on neuromuscular transmission. Ibogaine, in spite of its stimulant properties, had

