

THE PSYCHEDELIC REVIEW

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A Uterine Stimulant Effect of Extracts of Morning Glory Seeds *

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The history, description and use of seeds of certain members of the Convolvulaceae for divinatory purposes has been well documented in the literature by Schultes and Wasson.^{1 2} These reports have prompted several investigations, and recently Hofmann *et al.*^{3 4 5} have isolated and identified the active principles as certain ergot-type alkaloids. These are *d*-lysergic acid amide (ergine), *d*-isolysergic acid amide (isoergine), chanoclavine, elymoclavine and ergometrine. Further work by Taber *et al.*^{6 7 8} has established that the alkaloids are in the microbially sterile embryo. They have also reported that the leaf and stem, but not the root, of *Rivea corymbosa* also contained small amounts of alkaloids and that these principles are present in many varieties of morning glories. However, some of the seeds are listed only by horticultural name, and some are synonymous with others in his table of plants studied.

Our investigations⁹ indicate that the main psychotomimetic principles are limited to varieties or horticultural forms of *Ipomoea violacea* L. This would seem to make sense because, of the many different species of *Ipomoea* available to the Mexican natives in their local flora, only *Ipomoea violacea* L. is used in their religious ceremonies for divinatory purposes.

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THE PSYCHEDELIC REVIEW

The following is a list of morning glories we have studied botanically and chemically:

Botanical Name	Horticultural Name	Flower Color	Shows presence of indole alkaloids by thin layer chromatographic analysis as compared to authentic <i>Ipomoea violacea</i> and <i>Rivea corymbosa</i> seeds obtained from Mexico.
<i>Ipomoea violacea</i>	'Heavenly Blue'	Blue	Positive
" "	'Pearly Gates'	White	Positive
" "	'Flying Saucers'	Blue-white variegated	Positive
" "	'Wedding Bells'	Lavender	Positive
" "	'Summer Skies'	Light Blue	Positive
" "	'Blue Star'	Light Blue with dark blue midrib spears	Positive
<i>Ipomoea Nil</i>	'Scarlett O'Hara'	Red	Negative
" "	'Candy Pink'	Pink	Negative
<i>Ipomoea Nil</i> (From India)	—	Blue to violet	Negative
<i>Ipomoea muricata</i> (From India)	—	Blue to violet	Negative
<i>Ipomoea X Sloteri</i>	'Cardinal Climber'	Red	Negative
<i>Ipomoea hederacea</i>	—	Red	Negative
<i>Ipomoea lindheimeri</i>	—	Violet	Negative
<i>Ipomoea turpethum</i>	—	—	Negative
<i>Ipomoea maxima</i>	—	—	Negative

Gröger, who is presently studying the biogenesis of ergoline derivatives in *Ipomoea*^{10 11} has also reported the occurrence of these indole alkaloids in *Ipomoea* species.¹² He has stated that, for the first time, ergoline derivatives have been isolated from *Ipomoea rubro-caerulea* Hook. We believe that this species name is synonymous with *Ipomoea violacea* L. and that the plants may be identical. The name is listed as a synonym under *Ipomoea violacea* by House and Wasson.⁹ However, Gröger reported the presence of agroclavine and elymoclavine in *Ipomoea coccinea*, the first case of the presence of these ergot type alkaloids in this species.

The presence of ergonovine[†] in *Ipomoea* species has been reported by Taber,⁷ Gröger,¹² and Hofmann.¹³ Taber has detected it in 'Pearly Gates' and *Rivea corymbosa*, while Hofmann found it only in *Ipomoea violacea*.

[†]"Ergonovine" is synonymous with "ergometrine", Hofmann's designation.

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Shortly after the publication of these reports in the scientific literature, there arose in the United States a chewing-craze for morning glory seeds ('Heavenly Blue,' 'Pearly Gates,' 'Flying Saucers') for purposes of eliciting hallucinatory responses similar to LSD. Many articles followed in lay journals in the wake of these practices, further extending their usage. Many seed companies even reported depletion of their stocks of morning glory seeds.

In view of these developments and the fact that these readily available seeds contain ergonovine in quantities of around 0.005%,¹³ we became interested in testing the most popular varieties ('Heavenly Blue' and 'Pearly Gates') for possible oxytocic properties.

Tests by Savage *et al.*¹⁴ have shown that low doses (20 to 50 seeds of 'Heavenly Blue' and 'Pearly Gates') are capable of inducing "beginning imagery" and that higher doses (100 to 500 seeds) show distinct LSD-like effects. They produce spatial distortions and visual and auditory hallucinations as well as other effects characteristic of LSD.

A theoretical calculation based on the approximate weight of 4 grams per 100 seeds and a 0.005% figure for the amount of ergonovine in the seeds gives the following results:

Number of Seeds	Approximate amount of Ergonovine in milligrams (theoretical)
20	0.04
50	0.10
100	0.20
500	1.0

Although we have found that the Mexican *Ipomoea violacea* seeds (seeds which Hofmann reports his 0.005% figure for ergonovine) weigh slightly more than half their horticultural forms per 100 seeds, the above figures, even at half-value, fall well into the human dosage range for ergonovine. This range is 0.2 to 0.5 mg of ergonovine as an oxytocic.¹⁵

Since the isolated rat uterus has been used for the bioassay of ergonovine, we decided to use this tissue for our tests. The uterus was prepared in the following manner:

Female rats were killed by a blow to the head and the uterus rapidly removed. One horn was used per experiment, and about 14 horns were used throughout the experiments. To obtain isotonic recordings a uterine horn was mounted vertically in a standard tissue bath (70 ml).

THE PSYCHEDELIC REVIEW

Aerated de Jalon's solution¹⁶ at 37.5°C was used to obtain a quiescent tissue. The movements of the uterus were recorded on a slow moving kymograph. After running the smoked drum to obtain a control tracing, the aqueous extracts were added.

Preliminary experiments with crude aqueous extracts of ground seeds proved inconclusive because of the coating effect of the mucilaginous preparation on the isolated uterus. A slight oxytocic effect was detected, but it was not notable. It was then decided that a crude total extract of the indole alkaloids from the seeds be used. This was prepared by Gröger's method¹² and involves the following steps:

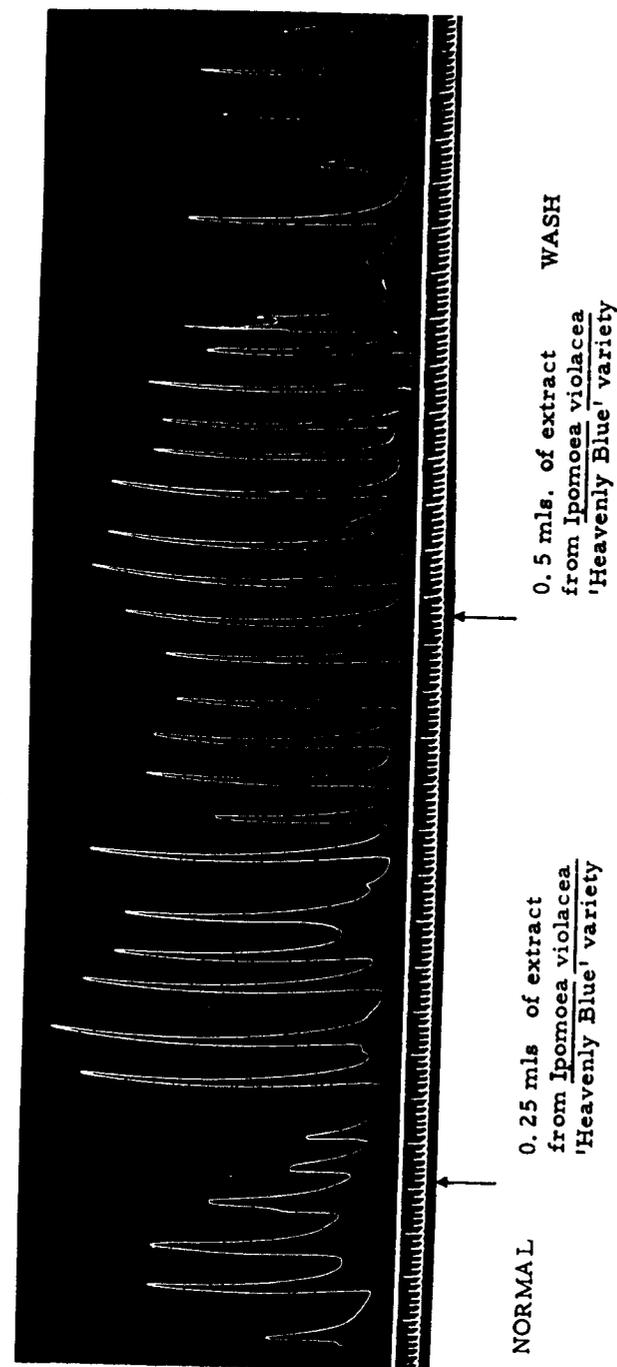
The ground seeds* were defatted with petroleum ether. This was followed by extraction with an acetone-tartaric acid solution. The acetone was evaporated off on a water bath, and the resultant tartaric acid solution was neutralized. This was finally extracted with methylene chloride to obtain the alkaloids. This was evaporated *in vacuo* and the extract taken up in 2 ml of water; aliquots were taken and added to the bath during normal rhythmic contractions. Several aqueous dilutions of each extract were used in the experiments. It was found that a 0.25 ml aliquot of the original 2 ml was capable of eliciting a maximal contractive response. This was approximately equivalent to a response effected by 0.1 ml of a 1 ml solution containing 0.2 mg of Ergonovine maleate (Ergonovine maleate, 0.2 mg/1 ml, ampoule, Lilly Co., Inc., Indianapolis, Indiana). After a few minutes, an additional 0.5 ml was added and a return to maximal contractions observed. This procedure was repeated with an extract of 'Badoh negro' (Mexican *Ipomoea violacea* seeds), 'Heavenly Blue' and 'Pearly Gates' (blue and white flowered varieties of *Ipomoea violacea*, respectively).

The results of one of these experiments with the 'Heavenly Blue' variety is shown in Fig. 1. Similar responses were seen in the case of all of these seeds.

A spectrophotometric chemical analysis by the Michelson and Kelleher¹⁷ modification of the Van Urk's assay was used to analyze the extracts. The 0.25 ml of the original 2 ml total extract which was used in the pharmacological tests, represents the following

*1 gram of seeds was used in each case.

FIGURE 1.
THE UTERINE STIMULANT EFFECT OF AN EXTRACT OF IPOMOEA VIOLACEA L.
SEEDS (MORNING GLORY 'HEAVENLY BLUE' VARIETY) ON ISOLATED RAT UTERUS



THE PSYCHEDELIC REVIEW

assayed amounts of total alkaloids calculated as ergonovine maleate:

<u>Name</u>	<u>Total alkaloids in 0.25 mls</u>	<u>% Total alkaloids in 1 gm of seeds</u>
'Badoh negro'	0.05 mg	0.040%*
'Heavenly Blue'	0.025 mg	0.024%
'Pearly Gates'	0.029 mg	0.024%

Since certain ergot-type alkaloids found in *Ipomoea* seeds are known to be oxytocic, due in part to their uterine-stimulant action, the authors suggest that a potential danger exists if excessive amounts are ingested. In addition, Savage¹⁴ has mentioned in his studies on humans the possibility of ergot poisoning with high doses of *Ipomoea* seeds.

*Hofmann reports 0.06% total with his collection of 'Badoh negro' (*Ipomoea violacea*) seeds. Our experience has shown that this total percentage varies from seed batch to seed batch. In addition, the thoroughness of extraction by various methods also varies.

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A Uterine Stimulant Effect Of Extracts Of Morning Glory Seeds*

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