

Voacanga Extraction Manual

Phase 1: Isolation of Total Alkaloids

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This procedure is to remain unpublished and under the control of Acidgaine LTD of Durban until August, 2015, when it becomes public domain.

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Background

The essentials of the procedure used in this manual were first developed for the isolation of *iboga* alkaloids in Paris in the mid 90s. At that time there was a need by a few ibogaine treatment providers for a method to efficiently isolate the alkaloids from *Tabernanthe iboga* root which could be followed without requiring training as a chemist. Using the 1957 method of Dickel as the best available guide, extraction was attempted by a series of publicly available solvents before observing that simply boiling powdered root with dilute lemon juice seemed to effectively separate the alkaloids. An inability to filter this extract led to departing from the highly conventional practice of heating during extraction, and later extensive testing to verify that the extraction at room temperature is still efficient. The other remarkable outcome was that making the filtered extract basic with ammonia led to a stable solid precipitate of total alkaloid (TA) which could be filtered, dried, powdered and stored. What had been expected based both on theory and previous extraction attempts was an unstable oil requiring solvent extraction and evaporation to isolate. Apparently it is components in the TA besides those structurally similar to ibogaine which gives it its solid properties, just as the protein in macadamia nuts renders them solid despite being over 50% liquid oil.

In Italy in 1998 the procedure from Paris was tested, optimized using white vinegar for extraction and compared with alternatives to complete a paper published in 2002 which includes refinement of the TA to a purified TA hydrochloride (PTA HCl) and to crystalline ibogaine HCl by recrystallization. The PTA HCl is precipitated from an acetone extract of TA using concentrated hydrochloric acid, as described by Dickel. Significant amounts of useful alkaloids remain dissolved in the acetone and can be recovered by evaporating the acetone, dissolving the residue in water and precipitating with base. Again, it is remarkable that a stable solid is obtained in this case also.

Also published in the 2002 paper was a procedure for isolating the TA from *Voacanga africana* bark with conditions and an outcome identical to that for *iboga* bark except that the yield tends to be higher. Further attempts to isolate the voacangine from the TA to convert into ibogaine were unsuccessful, mainly because of the relatively small proportion of voacangine in *Voacanga* TA compared with the high proportion of ibogaine in *iboga* TA. The inspiration to utilize *Voacanga* as an ibogaine source was mainly a 1957 patent by Janot and Goutarel which argued that *Voacanga* trees were more plentiful than *iboga* and could have bark harvested without destroying the trees.

Since 2002 the main advances in this area of chemistry have been the use of stronger acids for the bark extractions, especially important for *Voacanga* given the weakly basic nature of voacangine, and an elaborate but low-tech and inexpensive procedure for the refinement of the voacangine. The only other facility known to process *Voacanga* bark at this time is one in Chennai, India owned by Phytostan Enterprises of Canada. According to its owner, Bob Sisko of New York, in a public presentation in 2009, their process starts with a very expensive extraction of powdered *Voacanga* bark with hot toluene. Apparently it is the difficulty of changing this procedure, whose approval was painstakingly won from the US FDA, and not its merit in comparison with the one enclosed herein, which accounts for its continued use by Phytostan. Many other significant suggestions for improvements and cost reductions have likewise not enjoyed adoption by Phytostan.

While the 2002 publication had the intended effect of increasing the availability of ibogaine treatment for addiction, it had the unfortunate consequence of accelerating the approaching extinction of the *Tabernanthe iboga* species. The purpose of this and associated manuals is to relax demand for *iboga* root by providing abundant ibogaine from an alternative cultivated source, and to allow new markets to enjoy the enhancement ibogaine can offer to addiction treatment by making it affordable to those markets. While most of the material in this manual has been released to the public domain, most recently at the 2012 GITA conference in Vancouver,

and improvements since that date and this manual itself are to remain unreleased until August, 2015 to allow Acidgaine time to recover money invested in this research.

Overview

Given the low cost of materials required for this procedure, most of the attention in this manual is given to the logistics of maximizing scale while minimizing labor. Since the technology is low-level and easily understandable, the reader is welcome to participate in imagining and implementing better manufacturing methods than those described here.

The alkaloid extraction basically involves stirring powdered *Voacanga* bark with dilute acid, filtering and pressing the extract through cloth, precipitation of the TA with base and filtering through cloth to collect the TA. The TA paste is then dried, weighed and ground to a powder.

The acids used so far have been either hydrochloric acid or nitric acid. Hydrochloric acid has the advantage of being probably the most readily available and least expensive strong acid. The main drawback of using hydrochloric acid is that there is no way to render the waste stream safe for plants, so the only sustainable way to dispose of it is in the ocean. Nitric acid may be more expensive and carries the extra hazard of forming explosive compounds in contact with some organic substances, but actually makes the waste stream into a good fertilizer. Since a *Voacanga* tree farm would be the ideal location for use of this manual, the ability to get value from all waste streams should be attractive. The base used to precipitate the TA should match the intent behind the acid – sodium hydroxide, the cheapest base – can be used with hydrochloric acid to form sodium chloride (table salt) while ammonia can be used with the nitric acid to form ammonium nitrate solution. Water quality is usually not a concern for this process because of the extensive refinement of the TA later.

The most labor intensive step of the entire refinement process is the extraction of the bark powder with dilute acid because this step requires handling the largest weight of materials. The first standard method of separating the extract from the bark required twisting and squeezing a cloth sack into which the mixture was poured. At larger scale, a cotton pillow case was substituted for the small sack. The selection of 25 liter buckets with a 100 cm circumference allowed snug fitting of 50 cm wide pillow cases. The most labor-intensive step, manual wringing of the bags, was avoided by making presses using the 25 liter buckets. Ideas for future scaling to extractions of a few hundred liters include using bedsheets instead of pillow cases and either pumping extract from underneath the sheet and/or pressing the sheet pneumatically or by other means. At very large scale an extended trough or silo may make sense.

The extraction process is more efficient when bark is extracted in series rather than in parallel or as a single batch. What this means is that root is divided between several buckets in a row and extract is moved from left to right, with fresh acid added to the left and finished extract removed at the right. This allows more efficient extraction than would have been obtained if all the bark had been extracted in a single larger bucket because of the removal of the most concentrated extract. The number of extractions should be optimized to stop when further extraction would no longer be cost effective given the economic circumstances of the specific laboratory. The number is normally between six and twelve. In the most efficient extraction process using buckets, the number of buckets will equal the number of extractions required and with each extraction, the oldest bucket of bark will be discarded and a new bucket of wet bark added to the other end of the row. This ensures maximum exhaustion of the alkaloid from every bucket of bark.

Pillow cases can also be used for filtration of the TA. A small amount of TA may pass through a pillow case at the beginning of a filtration and this can be recovered later. The pillow cases can and should be reused to

prevent any loss of adhering TA, though it may be necessary to wash them in dilute acid to restore their permeability. After filtration and rinsing, the pillow case should be drained on dry towels in a stream of warm air until the hard, dry TA ceases to decrease in volume or mass. The drying step is one of the most time and energy intensive steps in the process and can be improved by increasing the surface area of the TA by spreading, periodic chopping and turning, skillful adjustment of airflow, blotting with a rotation of towels and the addition of a silting agent such as diatomaceous earth before filtration.

As with all phases on this manual, note that the amounts in the procedure can be scaled to the amounts on hand, and the size of the equipment adjusted accordingly. The times and temperatures should not be scaled.

Receiving Bark

From the very first batch it is important for a laboratory to collect a minimum of data for each shipment of *Voacanga* bark processed. Even as soon as a shipment of bark is received it is wise to **weigh the package** to ensure that it is not significantly underweight. After weighing, the package should be immediately opened to **ensure that the contents are dry**, since leaving wet bark sealed could lead to its decomposition and destruction. Next the **identity and quality of the bark should be noted** – its appearance and smell compared to previous batches, consistency, moisture, the presence of foreign matter such as dirt or unfamiliar plant matter. Rocks or large pieces of wood should be especially noted due to the damage they can inflict on the mill. Finally, the bark should be removed from the package and the empty package reweighed to **determine the net weight received**. Any significant discrepancy with the weight purchased should be reconciled with the seller. **The bark should be dried if necessary** to allow the actual weight of bark received to be determined and to ensure effective milling. The net weight of bark received for processing should be *permanently recorded* to allow yield calculation and tracking.

Milling

The *Voacanga* bark should be milled as finely as possible to allow the most contact between the acid and the bark and maximum extraction of alkaloid. Ear protection and an effective dust mask should be used. Care should be taken to minimize loss of dust in this process. If loss of dust from the hammer mill itself is unavoidable it can be recovered by milling in an enclosed room, letting the dust settle and sweeping it – provided that precautions to prevent a dust explosion are taken by consistently stopping the mill before the dust level becomes unsafe. The filter selected for the mill should be the finest which gives product at a reasonable rate. If the mill is electric a circuit may need to be specially installed to handle the current drawn when the mill starts, as this may exceed the ten amperes most 220 volt circuits are designed to carry.

It may be advantageous to mill bark in the area it is harvested, before shipping, as that reduces the volume required to be shipped.

Disadvantages are that foreign material and adulteration will become more difficult to identify and only a portion can be easily dried to estimate excess moisture content.



After milling it is important to set aside a sample of at least one gram of milled bark for HPLC analysis of the

voacangine content of this particular bark shipment. This allows the efficiency of the extraction process to be determined and also tracks important variations in seasonal alkaloid production which should inform purchasing decisions. Finally, any problem with the product of the extraction procedure can be more effectively tracked down if the quality of the starting materials can be verified.

Preparation for Extraction

Each kilogram of bark to be processed will require:

Seven liters of water (about two to wet the bark and five for extraction)

30 mL of 55% nitric acid (0.35 mol at 11.64 M) or 35 mL of 32% hydrochloric acid (0.36 mol at 10.17 M)

40 mL of 25% ammonia (0.72 mol at 18 M) or 28.5 grams of sodium hydroxide (0.71 mol at 40 g/mol)

About one to three 25 liter buckets, depending on whether presses made of buckets are used

If 25 liter plastic buckets are to be used for extraction, it is most efficient to load each bucket with 2.5 kg of bark. If a batch process is to be used, the best number of buckets is four to six. If a continuous process is used, the number of buckets should match the number of intended extractions, normally six to twelve. The bark can be weighed into each bucket. The exact weight in each bucket is not crucial, but the total weight extracted in the run must be recorded to allow the yield to be calculated.

Batch Process

In the batch process, the bark is divided between several buckets (ideally four to six, but possibly as few as one) and the extract passed from bucket to bucket until all the buckets have been exposed to all the portions of acid. Keeping track of this process is made easier by numbering the buckets, keeping them in order by number, and writing down the time each extraction was started and each finished extract was basified.

For example, suppose that there are ten kilograms of *Voacanga* bark to be extracted, and resources sufficient to complete only six extractions. The bark could be divided between four buckets, each getting 2.5 kg of bark. The bark in each bucket should be wetted with five liters of water to keep liquid from being retained on the first extraction. Assuming we use hydrochloric acid for this process, we will need 35 mL/kg * 2.5 kg = 105 mL of concentrated hydrochloric acid diluted to 5 L * 2.5 kg = 12.5 liters for each extraction. It will also take 28.5 g * 2.5 kg = 71.25 g sodium hydroxide to basify each extract. The fresh, dilute acid goes into bucket #1 which gets thoroughly stirred with a stick. After an hour, bucket #1 gets briskly stirred again to suspend all the solids and immediately poured into a pillow case in a press. The extract is pressed from the root solid and poured into bucket #2, while the solids are returned to bucket #1 and extracted with a fresh 12.5 liters of dilute hydrochloric acid. Both buckets are stirred, left an hour, pressed, and the extract from bucket #2 goes into bucket #3. Here is the outline for the entire extraction process:

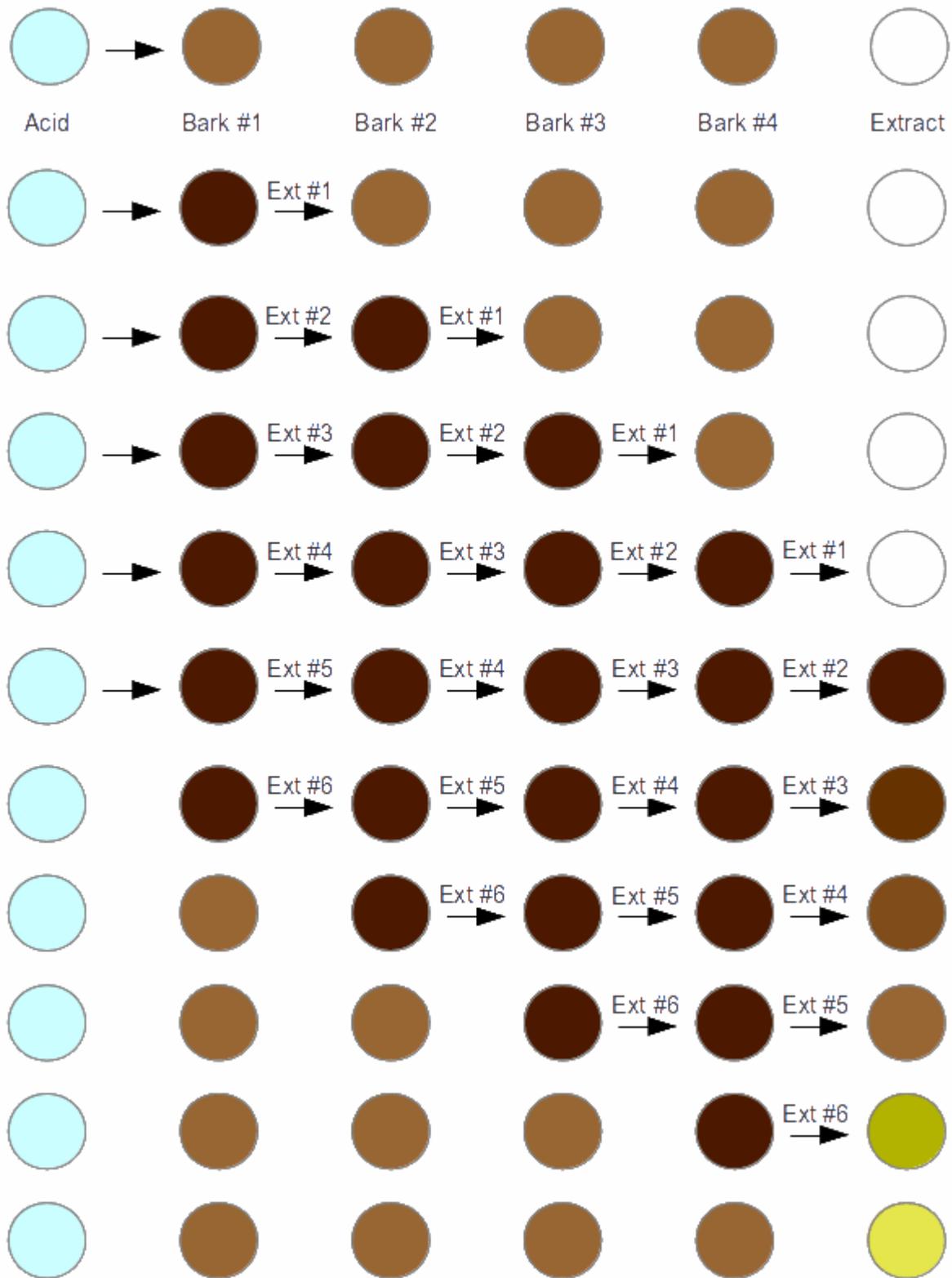
Extraction #1:

12.5 L dilute acid → bucket #1 (wait one hour)

Extraction #2:

Press extract from bucket #1 and put it in bucket #2

12.5 L dilute acid → bucket #1 (wait one hour)



Extraction #3:

Press extract from bucket #2 and put it in bucket #3
 Press extract from bucket #1 and put it in bucket #2
 12.5 L dilute acid → bucket #1 (wait one hour)

Extraction #4:

Press extract from bucket #3 and put it in bucket #4
Press extract from bucket #2 and put it in bucket #3
Press extract from bucket #1 and put it in bucket #2
12.5 L dilute acid → bucket #1 (wait one hour)

Extraction #5:

Press extract #1 from bucket #4, basify with 71.25 g sodium hydroxide and filter out the TA
Press extract from bucket #3 and put it in bucket #4
Press extract from bucket #2 and put it in bucket #3
Press extract from bucket #1 and put it in bucket #2
12.5 L dilute acid → bucket #1 (wait one hour)

Extraction #6:

Press extract #2 from bucket #4, basify with 71.25 g sodium hydroxide and filter out the TA
Press extract from bucket #3 and put it in bucket #4
Press extract from bucket #2 and put it in bucket #3
Press extract from bucket #1 and put it in bucket #2
12.5 L dilute acid → bucket #1 (wait one hour)

Press extract #3 from bucket #4, basify with 71.25 g sodium hydroxide and filter out the TA
Press extract from bucket #3 and put it in bucket #4
Press extract from bucket #2 and put it in bucket #3
Press extract from bucket #1 and put it in bucket #2
Discard the spent bark in bucket #1 (wait one hour)

Press extract #4 from bucket #4, basify with 71.25 g sodium hydroxide and filter out the TA
Press extract from bucket #3 and put it in bucket #4
Press extract from bucket #2 and put it in bucket #3
Discard the spent bark in bucket #2 (wait one hour)

Press extract #5 from bucket #4, basify with 71.25 g sodium hydroxide and filter out the TA
Press extract from bucket #3 and put it in bucket #4
Discard the spent bark in bucket #3 (wait one hour)

Press extract #6 from bucket #4, basify with 71.25 g sodium hydroxide and filter out the TA
Discard the spent bark in bucket #4

The TA from each of the six extracts can be filtered separately if it is important to track the yield or composition of each extraction. After filtration the TA should be rinsed with water, drained and dried.

Continuous Process

The continuous process uses the same concepts as the batch process but is intended to optimize extraction efficiency in the case where the supply of bark on hand to be processed is much larger than could be processed in a single batch. Assuming that eight extractions were to be performed per bucket of bark, the initialization of the Continuous Process would be identical to the Batch Process up to Extraction #6 and then continued for two more extractions, and only then discarding the bark in bucket #1 (hereafter called the leftmost bucket). At that

point the Continuous Process can be continued indefinitely with these steps:

1. Place the empty leftmost bucket to the right of the rightmost bucket.
2. Place 2.5 kg of fresh bark in the new rightmost bucket and wet it with 5 liters of water.
3. Stir the buckets and wait an hour.
4. After an hour, press the extract from the second bucket to the right and put the extract in the rightmost bucket. Return the bark pulp to the original bucket.
5. Continue in the same manner until the extract has been pressed from the leftmost bucket. Return the bark pulp to the leftmost bucket.
6. Add 12.5 liters of dilute acid to the leftmost bucket.
 1. Press the extract from the rightmost bucket, basify and filter the TA. Return the bark pulp to the bucket.
 2. Press the extract from the next bucket to the left and add it to the rightmost bucket. Return the bark pulp to the bucket.
 3. Continue in the same manner until the extract has been pressed from the leftmost bucket.
 4. Discard the bark pulp that was pressed from the leftmost bucket.



Illustration 1: Accurate, timely records make the process smoother both today and tomorrow

Batch Process Data Sheet

Date extraction started: _____ Name of chemist overseeing extraction process: _____
Total weight of bark to be processed: _____ kg Number of buckets: _____
Acid type and concentration: _____ Volume used per extraction: _____ mL
Volume of water used for wetting per extraction: _____ L
Volume of water used for acid dilution per extraction: _____ L
Base type and concentration: _____ Base volume/weight used per extraction: _____ mL/g
Volume of water used to dissolve base per extraction: _____ mL

Extraction #1 start time: _____ Diluted acid strength: _____ % maximum
Filter tare weight: _____ g; Gross weight: _____ g; TA net weight: _____ g

Extraction #2 start time: _____ Diluted acid strength: _____ % maximum
Filter tare weight: _____ g; Gross weight: _____ g; TA net weight: _____ g

Extraction #3 start time: _____ Diluted acid strength: _____ % maximum
Filter tare weight: _____ g; Gross weight: _____ g; TA net weight: _____ g

Extraction #4 start time: _____ Diluted acid strength: _____ % maximum
Filter tare weight: _____ g; Gross weight: _____ g; TA net weight: _____ g

Extraction #5 start time: _____ Diluted acid strength: _____ % maximum
Filter tare weight: _____ g; Gross weight: _____ g; TA net weight: _____ g

Extraction #6 start time: _____ Diluted acid strength: _____ % maximum
Filter tare weight: _____ g; Gross weight: _____ g; TA net weight: _____ g

Extraction #7 start time: _____ Diluted acid strength: _____ % maximum
Filter tare weight: _____ g; Gross weight: _____ g; TA net weight: _____ g

Extraction #8 start time: _____ Diluted acid strength: _____ % maximum
Filter tare weight: _____ g; Gross weight: _____ g; TA net weight: _____ g

Extraction #9 start time: _____ Diluted acid strength: _____ % maximum
Filter tare weight: _____ g; Gross weight: _____ g; TA net weight: _____ g

Extraction #10 start time: _____ Diluted acid strength: _____ % maximum
Filter tare weight: _____ g; Gross weight: _____ g; TA net weight: _____ g

Extraction #11 start time: _____ Diluted acid strength: _____ % maximum
Filter tare weight: _____ g; Gross weight: _____ g; TA net weight: _____ g

Extraction #12 start time: _____ Diluted acid strength: _____ % maximum
Filter tare weight: _____ g; Gross weight: _____ g; TA net weight: _____ g

Date extractions completed: _____ Total TA weight: _____ g

