DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: November 21, 2002

From: Division of Standards and Labeling Regulations, Office of Nutritional Products, Labeling and Dietary Supplements, HFS-822

Subject: 75-Day Premarket Notification of New Dietary Ingredients

To: Dockets Management Branch, HFA-305

New Dietary Ingredient:	*Desmodium adscendens* Swartz
Firm:	Biodynamics Nv
Date Received by FDA:	May 31, 2002
90-Day Date:	August 29, 2002

In accordance with the requirements of section 413(a) of the Federal Food, Drug, and Cosmetic Act, the attached 75-day premarket notification and related correspondence for the aforementioned new dietary ingredient should be placed on public display in docket number 95S-0316 as soon possible since it is past the 90-day date. Thank you for your assistance.

Catalina Ferre-Hockensmith

Attachments

95S-0316

RPT 135

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
College Park, MD

AUG 14 2002

Mr. Eric Maes
Biodynamics Nv
Joseph Plateaustraat 4
B-8400 Oostende
Belgium

Dear Mr. Maes:

This letter acknowledges receipt of a new dietary ingredient notification, dated May 21, 2002, you sent to the Food and Drug Administration (FDA) pursuant to 21 U.S.C. 350(a)(2). On May 31, 2002, FDA received and filed your notification concerning a substance that you assert is a new dietary ingredient that was identified by different names in your notification, including *Desmodium adscendens* Swartz, a perennial herbaceous plant commonly found in the African forest.

In accordance with 21 U.S.C. 350b(a)(2), a manufacturer or distributor of a dietary supplement that contains a new dietary ingredient must submit certain information to FDA at least 75 days before the dietary ingredient is introduced or delivered for introduction into commerce. This information must include the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such new dietary ingredient will reasonably be expected to be safe. FDA reviews this information to determine whether it provides an adequate basis for such a conclusion. Under section 350b(a)(2), there must be a history of use or other evidence of safety establishing that the dietary ingredient, when used under the conditions recommended or suggested in the labeling of the dietary supplement, will reasonably be expected to be safe. If this requirement is not met, the new dietary ingredient is deemed to be adulterated under 21 U.S.C. 342 (f)(1)(B), because there is inadequate information to provide reasonable assurance that the new dietary ingredient does not present a significant or unreasonable risk of illness and injury.

Your notification indicates that you want to market *Desmodium adscendens* Swartz in two physical forms under different product names. The product called "Desmodium" is described as a whole dry plant where the stems and leaves are to be used by the purchaser to make a water decoction for consumption. The product called "Desmopar®" is described as a prepared water decoction sold in ready-to-drink liquid form. Section 5 – Therapeutic Indications (pages 9-11) and Section 8 – Directions for Use (pages 13-14) of your notification describe in detail how Desmodium and Desmopar® are intended to be used to cure, mitigate, treat, or prevent several diseases, including: acute and chronic viral hepatitis; toxic hepatitis; fibrosis; allergies; asthma; minor hepatic dysfunction; and digestive disorders.

Under 21 U.S.C. 321(g)(1)(B), a drug is defined as an article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease. Therefore, your products Desmodium and Desmopar® containing *Desmodium adscendens* Swartz are drugs under 21 U.S.C. 321(g)(1)(B) and are subject to regulation under the drug provisions of the Federal Food, Drug and Cosmetic Act. If you wish these products to be evaluated for its use in the cure, mitigation, treatment of the diseases or disease conditions cited above, you should contact FDA's Center for Drug Evaluation and Research, Office of Compliance, HFD-310, 7520 Standish Place, Rockville, Maryland 20855.

In conclusion, your notification represents *Desmodium adscendens* Swartz as a drug and the notification is incomplete as described below. Consequently, there is an inadequate basis to conclude that the use of a dietary supplement that contains *Desmodium adscendens* Swartz will reasonably be expected to be safe. Therefore, your product may be adulterated under 21 U.S.C. 342(f)(1)(B) as a dietary supplement that contains a new dietary ingredient for which there is inadequate information to provide reasonable assurance that it does not present a significant or unreasonable risk of illness or injury. Introduction of such products into interstate commerce is prohibited under 21 U.S.C. 331(a) and (v).

Your notification will be kept confidential for 90 days after the filing date. Therefore, after August 29, 2002, the notification, its addenda and related correspondence from FDA will be placed on public display at FDA's Dockets Management Branch in docket number 95S-0316. However, any trade secret or otherwise confidential commercial information that is in the notification will not be disclosed to the public.

Prior to August 29, 2002, you may wish to identify in writing specifically what information you believe is proprietary. Nevertheless, our Center's Freedom of Information Officer has the authority to make the final decision about what information in the notification should be redacted before it is posted at Dockets.

It is possible for you to resubmit your information, after removing all drug claims, as a new notification for a new dietary ingredient. If you choose to resubmit, we offer the following comments on the deficiencies in your current submission. The notification you sent us concerning *Desmodium adscendens* Swartz is incomplete and does not provide the minimum information required under 21 CFR 190.6 for a new dietary ingredient notification. We have enclosed a copy of this section of the CFR for your future reference. You also may wish to review our FDA's Web site at http://www.cfsan.fda.gov/~dms/ds-ingrd.html for addition details on new dietary ingredient notification requirements. Your notification does not comply with 21 CFR 190.6 requirements because, in addition to making disease claims, it fails to:

- Confirm the complete Latin binomial name of plant used as the source of the new dietary ingredient, which includes the name(s) of the author(s) who validly described and published the plant name. We noticed in your notification that you spelled the new dietary ingredient two different ways: *Desmodium adscendens* Swartz, and *Desmodium abscendens.* To our knowledge and to conform to internationally accepted rules of botanical nomenclature, *Desmodium adscendens* (Sw.) DC. is the

correct way to state the genus and species of the plant that we believe is the subject of your notification.

- Clarify the recommended serving size of the dietary supplement containing the new dietary ingredient when Desmodium whole dry plant is used to prepare a decoction. It is unclear as currently presented if as much as 1-1/2 liters is the recommended serving size during a 24-hour period. In addition, page 12 of the notification states that the daily dose for adults of Desmopar® in liquid form is "20 ml in two doses." It is unclear to us whether this means two 10 ml doses daily or two 20 ml doses daily for adults.
- Identify any subgroups (e.g., by age, gender, or special circumstances like pregnancy, lactation, health status or use of medications) that should be excluded from the population of consumers.
- Submit three copies of the notification (i.e., an original and two copies). You only submitted a single copy.
- You have not presented any information establishing the basis for your determination that your material will reasonably be expected to be safe under the stated conditions of use, as is required by 21 CFR 190.6(b)(4).
- Provide copies or reprints of the articles listed in the bibliography on page 15 of your notification that were used in support of your determination that the new dietary ingredient is reasonably expected to be safe when used as indicated in the product's labeling. If any part of this information is in a foreign language, it must be accompanied by an accurate and complete English translation.

If you have any questions concerning this letter, please contact me at (301) 436-2371.

Sincerely yours,

Felicia B. Satchell

Felicia B. Satchell
Director
Division of Standards
and Labeling Regulations
Office of Nutritional Products, Labeling
and Dietary Supplements
Center for Food Safety
and Applied Nutrition

Enclosure

[Code of Federal Regulations]
[Title 21, Volume 3]
[Revised as of April 1, 2001]
From the U.S. Government Printing Office via GPO Access
[CITE: 21CFR190.6]

[Page 569-570]

TITLE 21--FOOD AND DRUGS

CHAPTER I--FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES (CONTINUED)

PART 190--DIETARY SUPPLEMENTS--Table of Contents

Subpart B--New Dietary Ingredient Notification

Sec. 190.6 Requirement for premarket notification.

(a) At least 75 days before introducing or delivering for introduction into interstate commerce a dietary supplement that contains a new dietary ingredient that has not been present in the food supply as an article used for food in a form in which the food has not been chemically altered, the manufacturer or distributor of that supplement, or of the new dietary ingredient, shall submit to the Office of Nutritional Products, Labeling and Dietary Supplements (HFS-820), Center for Food Safety and Applied Nutrition, Food and Drug Administration, 5100 Paint Branch Parkway, College Park, MD 20740, information including any citation to published articles that is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such dietary ingredient will reasonably be expected to be safe. An original and two copies of this notification shall be submitted.

(b) The notification required by paragraph (a) of this section shall include:

(1) The name and complete address of the manufacturer or distributor of the dietary supplement that contains a new dietary ingredient, or of the new dietary ingredient;

(2) The name of the new dietary ingredient that is the subject of the premarket notification, including the Latin binomial name (including the author) of any herb or other botanical;

(3) A description of the dietary supplement or dietary supplements that contain the new dietary ingredient including:

(i) The level of the new dietary ingredient in the dietary supplement; and

(ii) The conditions of use recommended or suggested in the labeling of the dietary supplement, or if no conditions of use are recommended or suggested in the labeling of the dietary supplement, the ordinary conditions of use of the supplement;

(4) The history of use or other evidence of safety establishing that the dietary ingredient, when used under the conditions recommended or suggested in the labeling of the dietary supplement, will reasonably be expected to be safe, including any citation to published articles or other evidence that is the basis on which the distributor or manufacturer of the dietary supplement that contains the new dietary ingredient has concluded that the new dietary supplement will reasonably be expected to be safe. Any reference to published information offered in support of the notification shall be

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accompanied by reprints or photostatic copies of such references. If any part of the material submitted is in a foreign language, it shall be accompanied by an accurate and complete English translation; and

(5) The signature of the person designated by the manufacturer or distributor of the dietary supplement that contains a new dietary ingredient.

(c) FDA will acknowledge its receipt of a notification made under section 413 of the Federal Food, Drug, and Cosmetic Act (the act) and will notify the submitter of the date of receipt of such a notification. The date that the agency receives the notification submitted under paragraph (a) of this section is the filing date for the notification. For 75 days after the filing date, the manufacturer or distributor of a dietary supplement that contains a new dietary ingredient shall not introduce, or deliver for introduction, into interstate commerce the dietary supplement that contains the new dietary ingredient.

(d) If the manufacturer or distributor of a dietary supplement that contains a new dietary ingredient, or of the new dietary ingredient, provides additional information in support of the new dietary ingredient notification, the agency will review all submissions pertaining to that notification, including responses made to inquiries from the agency, to determine whether they are substantive and whether they require that the 75-day period be reset. If the agency determines that the new submission is a substantive amendment, FDA will assign a new filing date. FDA will acknowledge receipt of the additional information and, when applicable, notify the manufacturer of the new filing date, which is the date of receipt by FDA of the information that constitutes the substantive amendment.

(e) FDA will not disclose the existence of, or the information contained in, the new dietary ingredient notification for 90 days after the filing date of the notification. After the 90th day, all information in the notification will be placed on public display, except for any information that is trade secret or otherwise confidential commercial information.

(f) Failure of the agency to respond to a notification does not constitute a finding by the agency that the new dietary ingredient or the dietary supplement that contains the new dietary ingredient is safe or is not adulterated under section 402 of the act.

[62 FR 49891, Sept. 23, 1997, as amended at 66 FR 17359, Mar. 30, 2001]

QUALITY HEALTH CARE PRODUCTS

21/05/02, Oostende

Dear Sir,

We'd like to notify the following 'new' dietary ingredient :
Desmodium Abscendens

We would like to export this product to the United States :
Biodynamics Nv
Joseph Plateaustraat 4
B-8400 OOSTENDE
BELGIUM
Tel. +32 59 805824
Fax +32 59 807812
Contact person : Maes Eric

Please find enclosed all the necessary info concerning the product called 'Desmodium Abscendens'.

We thank you in advance for your cooperation.

Yours sincerely,

Eric Maes
Biodynamics Nv

DESMODIUM
DESMOPAR®

DESMODIUM ADSCENDENS

DESMODIUM (dry plant for decoction) and DESMOPAR® ("ready to drink" form) are two presentations of *Desmodium adscendens*, an African plant used in traditional African medicine.

Pharmacological studies show its hepato-protecting effect, especially through its positive action on transaminases.

The product has no toxicity and is well tolerated.

Its main indications are **viral and toxic hepatitis**

⇒ **The more rapidly hepatitis is treated with DESMODIUM - DESMOPAR®, the more complete and permanent results are observed.**

Let's emphazise the fact that, according to our present observations. an early treatment with **DESMODIUM** or **DESMOPAR® avoids an acute hepatitis to change into a chronic one**.

Yet, when the chronic stage is reached, very interesting results are still obtainable.

C hepatitis is a special case, results are much more variable (more especially as the acute phase is often a silent one). Some very positive reactions have been observed as well as some complete failures.

Another successful indicaton is to **prevent hepatic side effects of drugs. DESMODIUM - DESMOPAR®** is recommended with chemotherapy to act before the foreseeable deterioraton and, more generally, whenever **the focus of prescription is to prevent hepatic deteriorations**.

CONTENTS

1 - HISTORICAL REVIEW

Desmodium adscendens is a more or less perennial herbaceous plant. It belongs to the papillonaceous family.

Its geographic habitat is the equatorial belt. It's commonly found in the African forest, where it grows up by trunks of trees such as oil palm trees and cacao-trees, as well as in Latin America and Asia. So *Desmodium adscendens*t can be picked up with no ecological risk.

In Africa, the plant is used by traditionnal practitionners in the treatment of various hepatic diseases including virus hepatitis.

Through a bibliographical research, one can observe that various indications are mentionned :

- in Ghana, the Center of Scientific Research into Plant Medecine uses stens and leaves to treat patients with asthma[(1)];
- in Cameroon, Ivory Coast and Senegal, according to "La flore du Sénégal", *Desmodium adscendens* is a treatment of stomach ulcers, constipation, etc...[(2)].

2 - BOTANICAL FILE

DESMODIUM ADSCENDENS SWARTZ is a more or less perennial herbaceous plant which grows up against the trunks of trees such as oil palm trees and cacao trees.
Plants used : stems and dried leaves
Origin of the plant SIERRA LEONE – NIGERIA - GHANA...
- wild plant
- Time of harvest : after flowering
- No treatment

2.1 DESCRIPTION OF THE PLANT DRUG

Macroscopically : - slim stems with hairs attached to them at intervals, those stems have fine roots exposed to the open air.
alternate trifoliated leaves, 15 to 50 mm long oboval leaflets, 10 to 30 mm wide, the central leaflet is more developed than the lateral ones, the base is rounded at the corner, the top rouned. 5 to 7 lateral veins. Hairless upperside or hairs sparsely scattered ; the underside more thickly covered in hairs which gives a lighter colouring to the lower side.
Beneath fine, slightly protruding reticulation.

Microscopically cf the cross transverses accompanying these notes and the photographs taken after the double classical colouring which shows the cellulose tissues in pink and the ligneous suberus and sclerenchymatous tissues in green. The stem presents : beginnings of lignification which is shown by the appearance of secondary tissues =
at the cortical level, the presence of suber 5 to 6 cell strata
at the central cylindrical level the presence of wood of slight thickness.

Same cellulose tissues like the phloema are fragile in this species and are easily crushed when cut. Pockets of pearly cellulose fibres are to be found in the cortical parenchyma. The beginnings of collenchyma appear under the suber. The medullary parenchyma is for the most absent. The leaf presents :
A pronounced ligneous arc accompanied by a non-inverted pocket of cribovascular tissue under the upper epiderm of the main vein.
This arc is accompanied by pink primary phloem pockets submerged in a sclerified parenchyma. Two of these phloem pockets are in inverted positions.
Relatively long hairs which we suppose exist through the presence of stumps on the surface and by some traces which we found in samples
2 strata of palissadic parenchyma.
These microscopic tests, after colouring, can be used to check the identity of the plant from onebatch to another.

3 – ANALYTICAL STUDY

3.1 Dose of the main components

Dose of alkaloids of the indolic type (the only known alkaloids in this genre and found in the Desmodium adscendens) expressed in relation to standard solutions of tryptamine.

Chromatographical techniques used : Chromatography of an extraction on a Extrelut 20 cartridge containing silica and elution with a – Isopropanol methylene chloride mixture (15/85 v/v).
Chromatography in thin layer on silica plates.
Mobile phase : methylacetate – Isopropanol – ammonia (45/35/20 in volume).

Desmodium adscendens contains around 8 mg/Kg of plant and the Desmodium decoction only contains traces ie 0,025 mg/L.

- Dose of mineral substances : .8 g/Kg
- Dose of total nitrogen : 12, 9%
- Dose glucides : none
- Dose of free amino-acids, the richness in proline and in amino-diacids can be noted. The total amount of proteins in the plant are characterized by a high content of these aminoacids as well as asparagine and tryptophane.
- Dose of fat acids which reach 3% of the total plant and are relatively rich in C18 insaturated acids.
- There is no oil essence.

Only the alkaloid dose & flavonoids (isovitexine) detection will be kept, the other components sharing nothing specific.

- Dose of ashes : 7%
- Humidity percentage : 10%
- Research of foreign elements by macroscopic examination.
- Research of falsifications is carried out at the game time as the alkaloid dose, which alkaloids should all belong to the family of indolic alkaloids.
- Dose of phytosanitary organochlorinated and organophosphorylated products. This dose was carried out at the L.A.R.A. 75, Voie du TOEC – 31300 TOULOUSE – this laboratory is equiped to carry out this kind of analysis : chromatography in the gaseous phase, equiped with a specific detector of flame photometer.

3.2 Estimation of microbiological cleanliness :

- by means of macroscopic examination during packaging and also by examining under a magnifying glass stems and leaves taken at random while pachaging.
Sinoe the conservation of the plant in jute bags in a dry airy place is excellent, decontamination is not foreseen but rather the rejection of a batch which might be contaminated.
The packagine is dosed manually by weighing 50 g of the plant in paper bags ; the upper part of the bag is folded twice and stapled three times. A slight movement of the hand will open the bag.

4 - PHARMACOLOGY/TOXICOLOGY -

4.1 PHARMACOLOGY

Pharmacological experimentations has been realised in two fields of activity :

- **antiallergic effect - In vivo action**

  This action has been shown up by ADDY and coll.

  Aqueous and ethanolic extracts of *Desmodium adscendens*, administrated per os, reduce the anaphylactic contractions, interfere with histamine-induced contractions, and reduce the amount of smooth muscle stimulating substances released from lung tissue of guinea pigs.. [3]

  Another study shows that three fractions (n-butanol, F2, and L5), isolated from an aqueous extract of *Desmodium adscendens*, a plant used in Ghana for the management of asthma, were evaluated for their pharmacological activity using ovalbumin and arachidonic acid-induced contractions of guinea pig airways. The results suggest that *D. adscendens* contains several pharmacologically active substances that can inhibit allergic airway smooth muscle contraction at multiple sites, including the synthsis and (or) activity of the bronchoconstrictor leukotrienes. [4]

  Another study shows that *Desmodium adscendens* inhibits the contraction of smooth muscles on a Guinea pig's separated ileum; these contractions having been induced by ovalbumin used as an allergenic agent. [5].

- **Hepato-protective effect - In vivo action**

  The hepato-protecting effect of *Desmodium adscendens* was evaluated on the rat with the carbon tetrachlorure test [6]..
  An positive action on transaminases is shown : the administration per os, during 4 days, of a lyophilisat of *Desmodium adscendens* decoction (equivalent 100 mg dry plant per kg) induces a significant dicrease of alanine-aminotransferase.

4.2 TOXICOLOGY

Let's first remind that *Desmodium adscendens* is very frequently used in traditional African Medecine (mainly in Ghana, Senegal; Cameroon and Ivory Coast) and no toxicity has ever been reported.

3 toxicology expertises, carried out in France, confirm that the plant is non-toxic :

- No acute toxicity - Estimation of acute toxicity (DL50) by feeding up rats [7].
- no mutagenic action -
  - Micronucleus test on the mouse [8]..
  - Reverse mutation test by means of Ames test. [9]

5 - THERAPEUTIC INDICATIONS

Main indications : Hepatitis

Viral hepatitis :
- **Acute phase**
- **Chronic B hepatitis**
- Chronic C hepatitis

Toxic hepatitis

Prevention of side effects of drugs on hepatic cells

can also be proposed in

- allergies/asthma

- liver complaints - minor hepatic dysfunctioning

-digestive disorders and stomach pains.

The animal experimentation have shown proof of *Desmodium adscendens* hepatic protective action[6]. So, it' easy to understand why the plant is efficient in virus hepatitis and, more generally, whenever liver cells are damaged, due to drugs administration, for instance with chemotherapy.

ACUTE VIRUS HEPATITIS

Virus hepatitis is a common - occasionally severe - disease which frequently entails asthenia and hepatic disorders over a short or longer period.

Up-to-now, there is no adequate curative treatment in the range of Western countries drugs (with exception of Interferon, costly treatment with well-known severe side effects.

This statement reinforces the interest of a therapy with *Desmodium adscendens* .

Desmodium adscendens (**DESMODIUM - DESMOPAR®**) gives excellent and rapid results when the symptomatology is characteristic of an "infectious icter", i.e. clinical symptoms such as jaundice, asthenia; modification of biological parameters such as transaminases, etc...

In these cases, even in the most severe ones, :

- icter and asthenia will disappear within a week;
- biological parameters (transaminases, bilirubin, etc;) will be back to normal, far much faster than without treatment, within 2 to 4 weeks.

A study about 32 observations of acute viral hepatitis shows that the effectiveness is rapid and permanent as soon as the hepatitis is treated in the first few days.

If the treatment is delayed, *Desmodium adscendens*' action will be less marked but partial results on the biological parameters can still be obtained.
The positive results are the same in A, B hepatitis or in accessory hepatitis observed with CMV or HIV patients.

In all cases, it seems that an early treatment prevents going into a chronic stage. No signs are observed for patients with a 3 to 8 years follow-up.

Special mentions :

- **C hepatitis** -

In theory, the results in acute C hepatitis are as good as in A or B hepatitis. However, if we stick to facts, results for C hepatitis are not so obvious because this disease, in its first stage, is often insidious and diagnosis occurs later on.

- **Auto-immune active hepatitis**
At this stage of hepatitis, *Desmodium adscendens* can still be administered but recourse to other immunomadulating treatments is necessary.
Good results have been observed with the association of **DESMODIUM - DESMOPAR®** and **SELONGENINE®** (Magnesium senegenate) - *Refer to SELONGENINE file*

CHRONIC VIRAL HEPATITIS

C and B hepatitis are mostly concerned.

In these cases, 3 parameters are to take in account for a good pronosis :

- **cytolysis evolutive outbreak**
There is an important increase in transaminases which shows the outbreak's severity.
DESMODIUM - DESMOPAR® permits to get the transaminases back to a non-preoccupating level (less than twice above normal rate) with a 3 weeks' treatment.

- **continued signs of viral presence**
They indicate a possible evolution towards cirrhosis or/and hepato carcinoma.

B hepatitis -
In France, in this indication, positive observations are reported.

These results are confirmed by a recent clinical trial of *Desmodium adscendens* (**DESMODIUM - DESMOPAR®**), in Mali, on 47 patients with B hepatitis [10]. This study shows a large.improvement of biological factors with a 45 days' treatment. Amino-transferase and bilirubin rates are reduced and more, for nearly half the patients (22 cases out of 47), Ag Hbs -virus' antigens- are cleared away.

C hepatitis

In Italy, a clinical preliminary study on C hepatitis [11] has recently been carried on with 41 patients (of which 20 with a suffisant follow up to be evaluated). It shows a improvement of hepatic functioning signs in 58% cases but also 26% complete failure.

In France. in the same indication, some cases of return to negative of viral RNA have been observed after a 6 to 8 weeks' treatment.

On the whole, one must say that results are variable.

- **Fibrosis**

In case of fibrosis, which is the main element of cirrhosis, **DESMODIUM - DESMOPAR®** is not to use alone.

In these cases - as in auto-immune phase hepatitis -, interesting clinical and biologicals results are obtainable with an association of **DESMODIUM/DESMOPAR®** *(Desmodium adscendens)* with **SELONGENINE®** (Senegenate de magnesium) - *Refer to SELONGENINE file*

TOXIC HEPATITIS

All toxic hepatitis, even severe, reacts perfectly to **DESMODIUM - DESMOPAR®**. These results are irrespective of etiology. They can be due to casual or to iatrogenic causes or due to the absorption of narcotics, to toxicomania (ethylism included).

For alcoholic pre-cirrhosis patients, stabilisation is obtainable if **DESMOPAR®** is used continuously with a discontinuous adjonction of **SELONGENINE®** (Senegenate de mg) - *Refer to SELONGENINE file*

PREVENTION OF SIDE EFFECTS OF DRUGS ON HEPATIC CELLS

Hepatic deteriorations (proved by transaminase rates) which may occur with chemotherapy are highly improved, both clinically and biologically.

It's still more valuable to act before the foreseeable deterioration. A preventive treatment will be associated to each chemotherapy period and in between if the hepato-digestive state makes it necessary.

6 - SIDE EFFECTS

Some rare cases of diarrhoea or nauseous state have been observed. These disorders stop as soon as the treatment is interrupted.

In many cases, it's only necessary to reduce the dose to get a good tolerance and so, to be able to go on with the benefit of treatment.

7 - PRESENTATIONS

- **DESMODIUM** - ***Desmodium adscendens*** **whole dry plant**
  Stems and leaves are cut in small bits, with the aim of producing a drinkable decoction.

  The daily dose is 10 g plant to be boiled during 15 minutes in water (1 ½ liter). After filtering, the decoction is to be drunk within the next 24 hours.

- **DESMOPAR®, the liquid form.**
  It's obtained from the decoction above mentionned, vacuum-concentrated and aromatized with oil of rosemary.

The daily posology will then be 20 ml in two doses for an adult and 3 ml per 10 kg for a child.

In other words, **20 ml DESMOPAR® are equivalent to 10 gr. of dry *Desmodium adscendens* plant.**

It's a "ready to drink" liquid. So, it's the easiest form, :
- for long term treatments (no daily preparation time needed)
- for children (less liquid to swallow).

and up to now, it's well tolerated, even by patients having met small problems with the decoction.

8 - DIRECTIONS FOR USE

8.1 POSOLOGY ACCORDING TO INDICATIONS

Virus hepatitis/toxic hepatitis

For all indications where hepatic cell is really damaged (increase of transaminases) :

- the daily posology will be :

  . either 10 g **DESMODIUM** dried plant (decoction prepared by boiling in 1 liter of water);
  . or "ready to drink "20 ml **DESMOPAR®**

  for an average 70 kg adult.

- treatment to be continued until symptoms are cleared away and biological factors back to normal, i.e. in acute disease, 2 to 6 weeks and in chronic ones, 6 to 8 weeks .

  Let's note that a recent Malian clinical trial in chronic B hepatitis [10] recommends, in order to confirm the return to normality of biological parameters, to extend the duration of treatment for one month or more.

Prevention of hepatic alterations with chemotherapy

In these indications, the dosage is reduced to two third of the conventional dose i.e. :

- daily posology - According to patient's preference,

  . either decoction prepared by boiling 6/7 g of **DESMODIUM** dried plant in 1 liter water
  . or "ready to drink "14 ml **DESMOPAR®**

- each cure will be seven days long, starting 2 days before chemotherapy;

- treatment will be continued between chemotherapies if the hepato-digetive state of patient makes it useful.

Allergies/asthma (or when the conventional dose is not well tolerated)

In these indications, the dosage is reduced to half the conventional dose i.e.

either decoction prepared by boiling 5 g of **DESMODIUM** dried plant in ¾ liter water

or "ready to drink "10 ml **DESMOPAR®**

for an average 70 kg adult.

8.2 RECOMMENDED METHOD OF PRESCRIPTION

- **MONOTHERAPY**
  in most cases,

- **ASSOCIATION WITH SELONGENINE® (Senegenate de magnesium)**
  - Auto-immune active hepatitis
  - Alcoholic pre-cirrhosis : **DESMOPAR®** continuously, **SELONGENINE®** discontinuously.
  - Fibrosis

The botanic analysis were carried out by Professor Max HENRY, Faculty of Pharmaceutic Sciences, 3, Avenue Jules Guesde – 31000 Toulouse.

The cuttings realised on the samples of «Desmodium adscendens», lot 11, show the basic characteristics of the species :

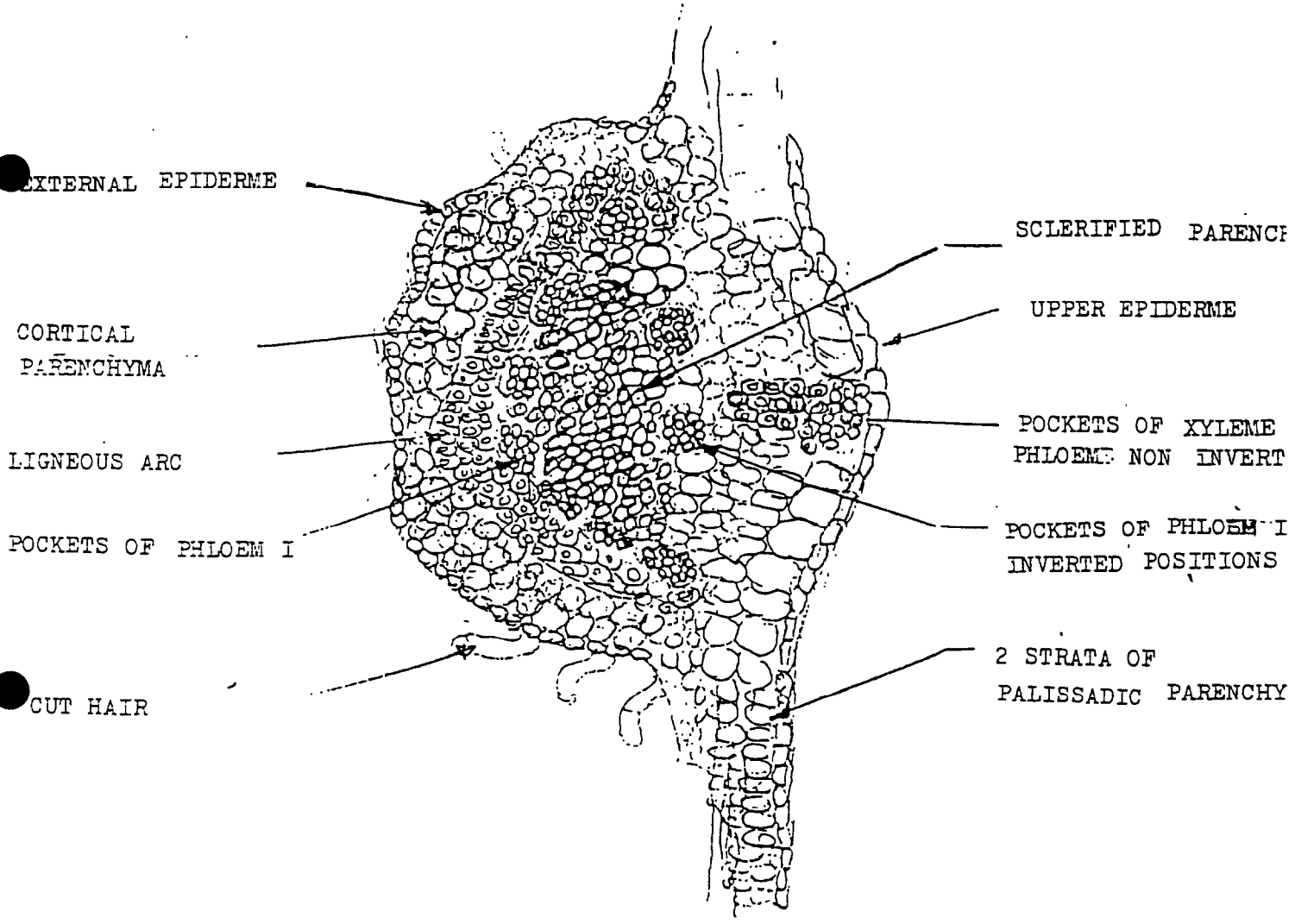
- At the stem one finds a suberification of the cortex, a lignification at the central cylinder and the presence of pokets of pearly fibres. In the present sample, these fibres are less sclerosed due to the fact that the plants are relatively young.

- At the leaves, the leaflets (folioles), in a cross tranversal position show the two pockets of phloem in typically inverted positions, characteristic of the species. Besides, there is a typical lignification at the tissues of the central principal nervure.

- At the roots, there are not any remarkable findings for the fragility of the tissues do not facilitate the realisation of the cuttings like the expert appraisement done before.

P.J. 4 plates of photos.

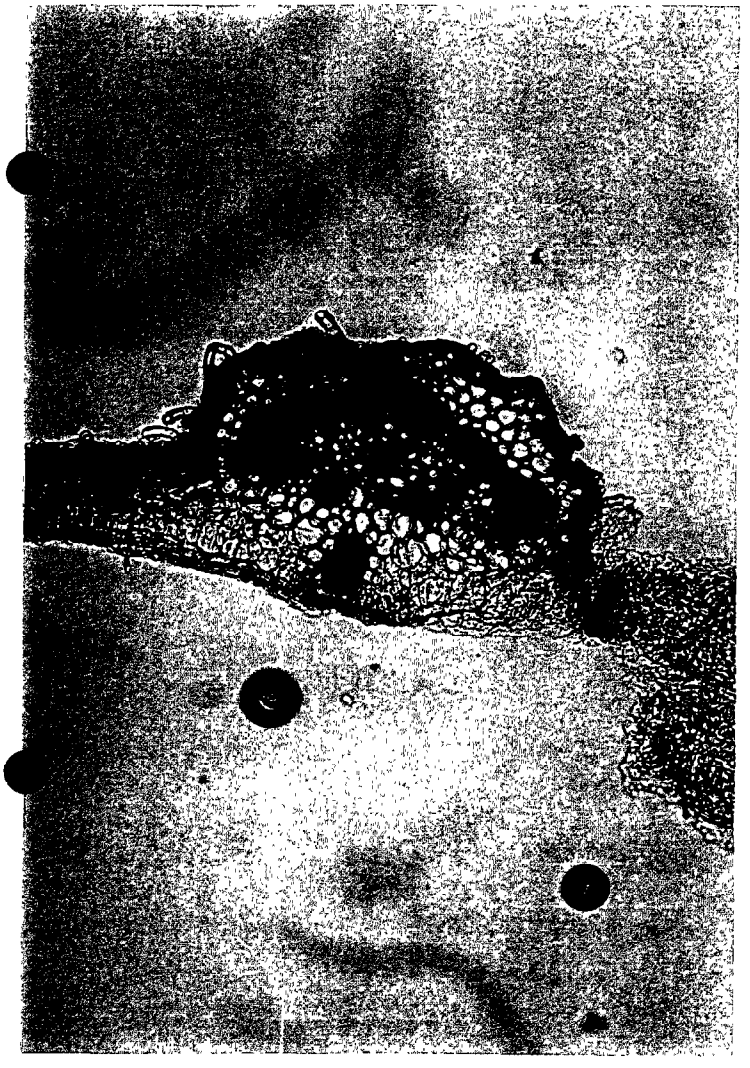
DESMODIUM ADSCENDENS (LEGUMINEUSES)



CROSS TRANSVERSE OF THE LEAF

DESMODIUM ASCENDENS (LÉGUMINEUSES)

COUPE TRANSVERSALE DE FEUILLE



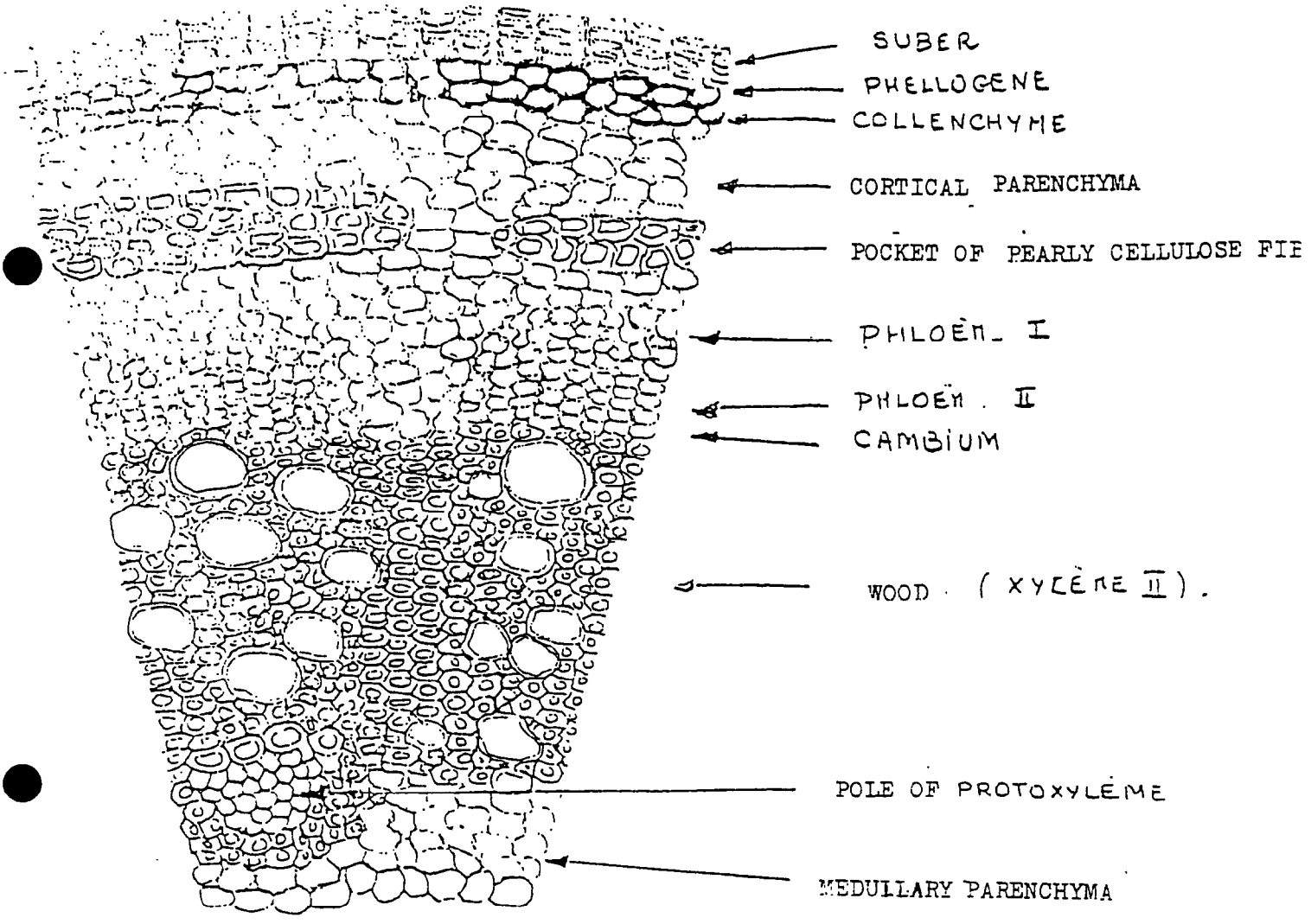
Objectif x 10

Nervure principale

Objectif x 40

Détail de l'arc libéro-ligneux

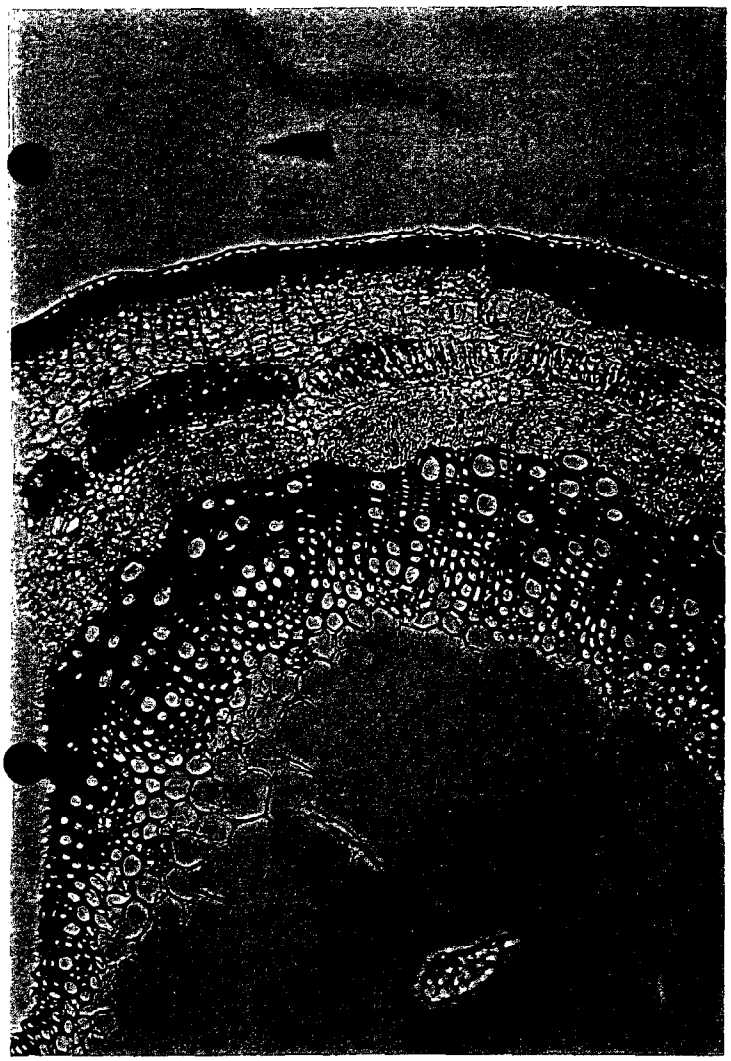
DESMODIUM ADSCENDENS



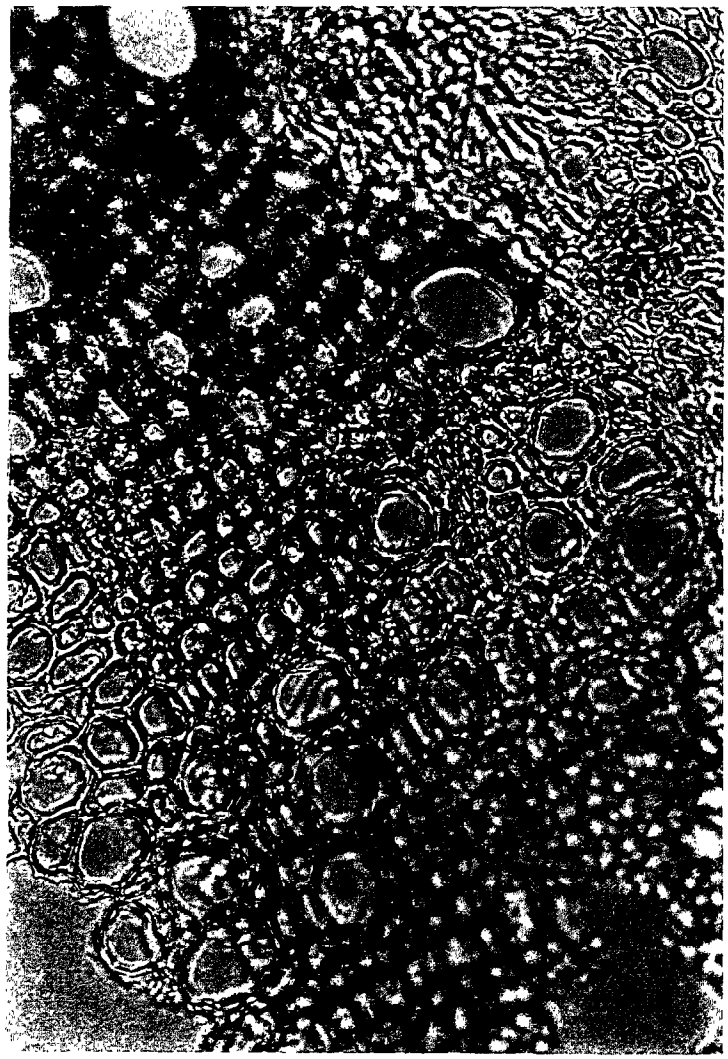
PART OF CROSS TRANSVERSE OF STEM

DESMODIUM ASCENDENS (LEGUMINEUSES)

COUPE TRANSVERSALE DE TIGE



Objectif x 10
Vue d'ensemble



Objectif x 40
Détail des tissus du bois.

CONTROL DATA SHEET

Product :	**DESMODIUM**	**Code**
Lot N°		**Quantity**
Attn		
Date		

		RESULTS	*REFERENCE*
1 - Visual research			
	- foreign substances		*< 2%*
	- moulds		*None*
2 - Identification			
	- macroscopic aspect		*Identical to identified samples*
	- microscopic aspect (colored stems and leaves)		
	- Isovitexine		*Presence*
	- tryptamine and derivates T.L.C.detection		*Presence*
3 - Dosages	- Ashes		*7 ≡ 1%*
	- % humidity		*10 = 2%*
	- Tryptamina and derivales		*8 = 2% mg/Kg*
	- Organophosphored		
	- Organochlored - HCH		
	- Lindane		*Conform to European pharmacopoeia*
	- DDE		
	- DDT		
	- Misc.		
4 - Bacteriological analysis			
	- Mould and yeasts		*$<2.10^{4}$/g*
	- Escherichia coli		*None*
	- Stahyloccocus Aureus		*None*
	- Salmonellae		*None*
	- Pseudomonas aeruginosa		*None*
	- Total aerobian germs		*$<2.10^{5}$/g*

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