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L'INITIATIVE DE
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DES CAPACITES
POUR L'APA

The ABS Compliant Biotrade in South(ern) Africa Project

Project Steering Committee Meeting
26 & 27 September 2018

Further information on Marula fruit
and oil and *Aloe ferox*
Recommendations

Cyril Lombard

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Marula fruit chemistry and health

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Marula traditional uses

Many uses across all ethnic groups where the resource occurs, truly a “transboundary” TK and IKS example

These include the fruit for food and beverages, and the kernel as a food and condiment, and the oils from the kernel as an emollient

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Sclerocarya birrea (Marula), An African Tree of Nutritional and Medicinal Uses: A Review

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Sclerocarya birrea (Anacardiaceae) is a popular African wild tree distributed in many African countries where the leaves, stem bark, root, and fruits are used in food and traditional medicine; the fruit is rich in ascorbic acid. The fruit juice contains sesquiterpene hydrocarbon, which are terpenes found in plants that are reported to have bacteriostatic properties. The fruit contains a hard brown seed. The seed encloses a soft white kernel rich in oil and protein. The oil contains oleic, palmitic, myristic, and stearic acids; the kernel protein contains amino acids, with a predominance of glutamic acid and arginine. The extracts from different parts showed high total phenolic compounds and radical-scavenging capacities and antioxidant activities. *Sclerocarya birrea* is widely studied with regard to its antidiabetic, anti-inflammatory, analgesic, antiparasitic, antimicrobial, and antihypertensive activities.

Keywords Antidiabetic, Anti-inflammatory, Antimicrobial, Antioxidant, Phenolic compounds, Protein, Oil, *Sclerocarya birrea*

Bark and roots include: “hypertension” and diabetes mellitus” as well as “anti-inflammatory conditions” (Ojewole, 2003) and “type 2 diabetes mellitus” (Ojewole, 2004)



Marula fruit chemistry and health



Available online at www.sciencedirect.com

ScienceDirect

Food Chemistry 103 (2007) 82–87

Food
Chemistry

www.elsevier.com/locate/foodchem

Phenolic composition of *Flacourtia indica*, *Opuntia megacantha* and *Sclerocarya birrea*

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J. Agric. Food Chem. XXXX, xxx, 000

Phenolic Antioxidants and Antiatherogenic Effects of Marula (*Sclerocarya birrea* Subsp. *caffra*) Fruit Juice in Healthy Humans

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BIANCA FUHRMAN,⁵ JUDITH ATTIAS,⁵ NINA VOLKOVA,⁵ TONY HAYEK,⁵ AND
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Southern Arava R&D, Mobile Post Hevel Eilat 88820, Israel, and Lipid Research Laboratory, Rappaport Faculty of Medicine, Technion–Israel Institute of Technology, Haifa 32000, Israel

Marula fruit chemistry and health

Thesis

Submitted in fulfilment of the requirements for the degree of doctor
at Wageningen University
by the authority of the Rector Magnificus
Prof. dr. M. J. Kropff,
in the presence of the
Thesis committee appointed by the Academic Board
to be defended in public
on Friday 25 October 2013
at 11 a.m. in the Aula

Penny Hiwilepo-van Hal

Processing of marula

**(*Sclerocarya birrea subsp. Caffra*) fruits:
A case study on health-promoting
compounds in marula pulp**

Convincing array of publications supporting a health positioning around the metabolic syndrome. Molecules and compounds such as phenols, polyphenols, catechins, epigallocatechins, flavonoids, seem to be responsible

This is supported by a body of grey and confidential literature

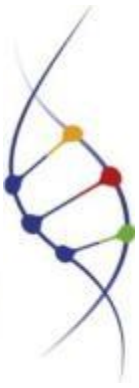
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***Sclerocarya birrea* (Marula), An African Tree of Nutritional and Medicinal Uses: A Review**

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Marula fruit chemistry and health

Table 2. Potassium content of Marula and other commonly consumed fruits

Fruit	K content (mg)	Fruit weight (g)
Marula flesh	1250	50
Marula Peel	900	50
Apricots (dried)	814	70
Banana	467	118
Dates	542	83
Kiwi	252	76
Melon, cantaloupe	494	160
Orange	237	131



Summary: EFSA Journal 2010; 8(2):1469

SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to potassium and maintenance of normal muscular and neurological function (ID 320, 386) and maintenance of normal blood pressure (ID 321) pursuant to Article 13(1) of Regulation (EC) No 1924/2006¹

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)^{2, 3}

BOX 1: European Food Safety Authority (EFSA) Claims

Scientific Opinion on the substantiation of health claims related to potassium and maintenance of normal muscular and neurological function (ID 320, 386) and maintenance of normal blood pressure (ID 321) pursuant to Article 13(1) of Regulation (EC) No 1924/2006

Muscular and neurological function

The claimed effects are “signal transduction and muscle contraction” and “nerve function”. The target population is assumed to be the general population. The Panel considers that maintenance of normal muscular and neurological function is a beneficial physiological effect. On the basis of the data presented, the Panel concludes that a cause and effect relationship has been established between the dietary intake of potassium and normal muscular and neurological function.

Blood Pressure

The claimed effect is “blood pressure”. The target population is assumed to be the general population. The Panel considers that maintenance of normal blood pressure is a beneficial physiological effect. On the basis of the data presented, the Panel concludes that a cause and effect relationship has been established between the dietary intake of potassium and the maintenance of a normal blood pressure.

It may be possible to position marula fruit products as “high in Kalium” / “high in Potassium”

Marula fruit – relevant patent

- EP: Withdrawn with legal effect as of April 2017, no divisionals
- US: Granted, claims limited to treatment of atherosclerosis, no divisionals
- IL: Granted
- RSA: Granted as filed with PCT

Option 1: Proceed, and if challenged by applicant we point out invalidity of claims, and possibly ABS issues too; they may seek to license, but they're in a weak position

Option 2: Challenge in court – but expensive

Option 3: To discuss...



(12) **United States Patent**
Borochov-Neori et al.

(10) **Patent No.:** **US 8,445,040 B2**
(45) **Date of Patent:** **May 21, 2013**

(54) **EXTRACTS OF *SCLEROCARYA BIRREA***

(75) Inventors: **Hamutal Borochov-Neori, Eilat (IL); Amnon Grinberg, Kibbutz Yotvata (IL)**

(73) Assignee: **Management and Holdings—Ardom, D.N. Eilat (IL)**

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **12/867,756**

(22) PCT Filed: **Feb. 19, 2009**

(86) PCT No.: **PCT/IL2009/000192**

§ 371 (c)(1),
(2), (4) Date: **Aug. 16, 2010**

(87) PCT Pub. No.: **WO2009/104184**

PCT Pub. Date: **Aug. 27, 2009**

(65) **Prior Publication Data**

US 2010/0311828 A1 Dec. 9, 2010

Fundira (J. Agric. Food Chem. (2002), vol. 50, pp. 1535-1542).
Mason (Vascular Health and Risk Management (2011), vol. 7, pp. 405-416).
Ndhala (Food Chemistry (2007), vol. 103, pp. 82-87—available online Oct. 2006).
Gorinstein (Journal of the Science of Food and Agriculture (2002), vol. 82, pp. 1166-1170).
Emborg (Journal of Neuroscience Methods (2004), vol. 139, pp. 121-143).
Mdluli, Kwanele, M., et al., "Enzymatic Browning in Marula Fruit I: Effect of Endogenous Antioxidants on Marula Fruit Polyphenol Oxidase," Journal of Food Biochemistry, (2003), pp. 67-82, vol. 27.
Pretorius, Victor, et al., "Volatile Flavour Components of Marula Juice," Z Lebensm Unters Forsch., (1985) pp. 458-461, vol. 181.
Borochov-Neori, Hamutal, et al., "Phenolic Antioxidants and Antiatherogenic Effects of Marula (*Sclerocarya birrea* Subsp. caffra) Fruit Juice in Healthy Humans," Journal of Agricultural and Food Chemistry, (2008), pp. 9884-9891, vol. 56.
Dimo, Théophile, et al., "Effect of *Sclerocarya birrea* (Anacardiaceae) stem bark methylene chloride/methanol extract on streptozotocin-diabetic rats," Journal of Ethnopharmacology, (2007), pp. 434-438, vol. 110.
Ojewole, John, A. O., "Evaluation of the Analgesic, Anti-inflammatory and Anti-diabetic Properties of *Sclerocarya birrea* (A. Rich.) Hochst. Stem-Bark Aqueous Extract in Mice and Rats," Phytotherapy Research, (2004) pp. 601-608, vol. 18.
International Search Report, International Publication No. WO 2009/104184 A3, International Application No. PCT/IL2009/000192, mailed on Oct. 28, 2009, 6 pages.

(57)

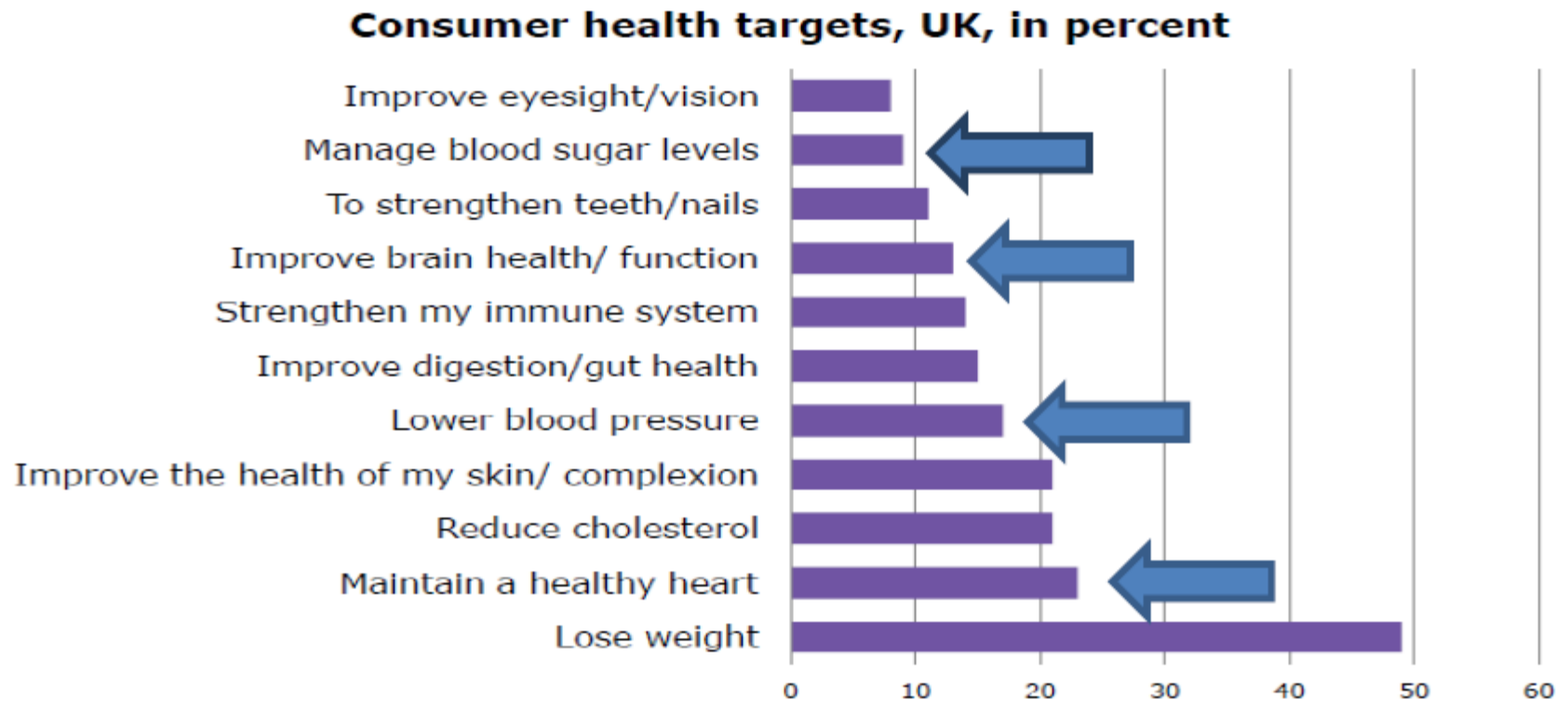
ABSTRACT

Provided are extracts obtained from the marula fruit (*Sclerocarya Birrea*) and uses thereof in a great variety of applications, e.g., use in food supplements for engendering an anti-atherogenic effect in healthy and non-healthy subjects (humans and non-human animals) and as agents for treating or preventing various diseases and disorders.

Marula fruit and potential consumer health targets



Figure 1: Possibilities for positioning marula fruit products in health sectors



Aloe ferox – market access regulatory issues

Aloe ferox: An initial market access and safety review, February 2014, PhytoTrade Africa, found numerous contradictory and uncertain positions for many product categories and territories. Usually the market access dossiers held by clients, not by producers in South Africa.

This means a whole category of products containing *Aloe ferox* could fall away – specialised advice required; project may need to focus of topical applications.

- MHRA – Products granted Traditional Herbal Registration (THR) which contain *A. ferox*
 - THR 00250/0220 Potter's Cleaning Herb Tablets
 - THR 00904/0005 Kerbina CASSILAX
 - THR 15670/0046 Napiers Sennamix Constipation Relief (specifies Cape Aloe leaf)
 - THR 15670/0044 Napiers Herbease Laxative Tablets (specifies Cape Aloe leaf)

Safety of hydroxyanthracene derivatives for use in food

EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS),
Maged Younes, Peter Aggett, Fernando Aguilar, Riccardo Crebelli, Metka Filipčič,
Maria Jose Frutos, Pierre Galtier, David Gott, Ursula Gundert-Remy, Gunter Georg Kuhnle,
Claude Lambré, Jean-Charles Leblanc, Inger Theresse Lillegaard, Peter Moldeus,
Alicja Mortensen, Agneta Oskarsson, Ivan Stankovic, Ine Waalkens-Berendsen,
Rudolf Antonius Woutersen, Raul J Andrade, Cristina Fortes, Pasquale Mosesso,
Patrizia Restani, Fabiola Pizzo, Camilla Smeraldi, Adamantia Papaioannou and Matthew Wright

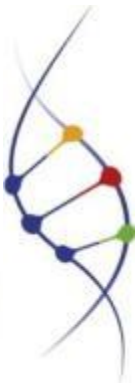
Abstract

The Panel on Food Additives and Nutrient Sources added to Food (ANS) was asked to deliver a scientific opinion on the safety of hydroxyanthracene derivatives and to provide advice on a daily intake that does not give rise to concerns about harmful effects to health. Hydroxyanthracene derivatives are a class of chemical substances naturally occurring in different botanical species and used in food to improve bowel function. The ANS Panel reviewed the available scientific data on a possible relationship between hydroxyanthracene derivatives exposure and genotoxic and carcinogenic effects. On the basis of the data currently available, the Panel noted that emodin, aloe-emodin and the structurally related substance danthron have shown evidence of *in vitro* genotoxicity. Aloe extracts have also been shown to be genotoxic *in vitro* possibly due to the presence of hydroxyanthracene derivatives in the extract. Furthermore, aloe-emodin was shown to be genotoxic *in vivo* and the whole-leaf aloe extract and the structural analogue danthron were shown to be carcinogenic. Epidemiological data suggested an increased risk for colorectal cancer associated with the general use of laxatives, several of which contain hydroxyanthracene derivatives. Considering the possible presence of aloe-emodin and emodin in extracts, the Panel concluded that hydroxyanthracene derivatives should be considered as genotoxic and carcinogenic unless there are specific data to the contrary, such as for rhein, and that there is a safety concern for extracts containing hydroxyanthracene derivatives although uncertainty persists. The Panel was unable to provide advice on a daily intake of hydroxyanthracene derivatives that does not give rise to concerns about harmful effects to health.

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derivatives, food supplements, genotoxicity, carcinogenicity, bowel
ives

Aloe ferox – patent review



Not a definitive “freedom to operate” report as that requires a high level of engagement with sector, and time/resources as there are many patents – more than 6,000 documents

Results : Aloe = 6,000
Aloe ferox = 42
Aloesin = 36, 7 families
Aloin = 117, 1 family

Search terms = Aloe, Aloe ferox, aloin and aloesin

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
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(25) Filing Language: English

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(30) Priority Data:
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(71) Applicant (for all designated States except US): **CSIR.**

(74) Agents: **SPOOR & FISHER** et al.; Building No. 13, Highgrove Office Park, Oak Avenue, Centurion, P O Box 454, 0001 Pretoria (ZA).

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(54) Title: METHOD FOR CONVERTING ALOERESIN A TO ALOESIN

(57) Abstract: The invention provides a process for hydrolytically converting aloeresin A to aloesin by the following reaction: The amount of aloesin available for extraction from sap of aloe plants is thereby increased and the extraction and purification of the aloesin is also made easier and less costly. As aloesin is more commercially valuable than aloeresin A, the process also increases the commercial value of the sap or aloe bitters from the aloe plant. The process optionally also includes the step of separating the aloesin from the p-coumaric acid. Typical hydrolysis steps that are used in the process are acid hydrolysis, base hydrolysis and enzymatic hydrolysis. In the case of acid hydrolysis, the acid is any suitable organic or inorganic acid, such as hydrochloric acid, sulfuric acid, nitric acid or phosphoric acid. In the case of enzymatic hydrolysis, the hydrolytic enzyme is typically an esterase, a lipase or a protease.

Many in Asia – skin lightening, numerous expired or dropped, worth looking at successful “Carrington family”

Recommendation on value chain selection



Based on reports presented in July and September: Project should now move more towards requiring SMEs and/or their support organisations to convince project management that the fundamentals of their respective value chains they work in are operable, and for the project to focus on identifying those SMEs and support organisations with credible business propositions. This approach allows for other value chains and species to be included if there are credible business cases presented to the project by industry.

Marula – yes – momentum with other institutions - candidate for Component 1.1 – weakness = no trade association, time to impact?

Essential oil cluster – yes – good fit with UNIDO project

Aloe ferox – yes – pay attention to regulatory risk reference EFSA – good fit with GEF6/UNDP project

Seed oil cluster – yes – good fit with UNIDO project, could add others like mafura at low additional cost?

Consider: Moringa – MDASA, growing market, diversification / domestication prospects

Consider: Baobab – growing market, dynamic support by African Baobab Alliance

Consider: Myrothamnus – SME support, growing market for herbal teas

Honeybush tea: Market, SAHTA, HCP, Grounded

Thank you

