

THE JOURNEY FROM AYURVEDA TO STANDARDIZED PHYTOEXTRACTS

Dr. Majeed Muhammed¹, Dr. Vaidyanathan Priti², Dr. Bhat Beena³

¹Founder and Managing Director, ²Senior Manager, ³Executive Vice-President, R&D-Phytochemistry;

Sami Labs Limited, # 19/1, 19/2, I Main, II Phase, Peenya Industrial Area, Bangalore, Karnataka, India

ABSTRACT

Innovative and natural, a synergistic combination of science & nature makes the ingredients used in Ayurveda very unique. While this form of medicine is still practised extensively across the country, its presence globally may be viewed as the efforts of a few concerned and who have seen success. This is because concepts involved in Ayurveda require effective translation through modern scientific approaches to present worldwide. Validation of phytoextracts with respect to their chemical composition and mechanisms of action form the fundamental requisites. Crucial steps in this entire process include the use of authenticated raw materials, identification of appropriate plant parts, standardization to known valid biomarkers and evaluation of safety and efficacy. It is the ethical responsibility of the scientific fraternity to take to the world quality Ayurveda based ingredients and formulations for betterment of human health. As a Health Science Company, the Sabinsa group integrates modern scientific techniques with ancient wisdom of Ayurveda to identify new molecules & health solutions that have brought back smiles to millions of families around the world. It provides consumers with the best of natural product solutions, derived from Ayurvedic concepts that are backed with science (modern techniques) for Health & Wellness in Life. With over 150 standardized phytoextracts to its credit, each of these products has made way into millions of dosage forms across the world. A few are outlined here for a better understanding of the journey of Ayurveda that has evolved into acceptable and preferred dosage forms.

Keywords: Ayurveda, scientific validation, safety, efficacy, holistic

INTRODUCTION

The Ayurveda is one of the earliest forms of medicine that is native to India. With its earliest mention in the literary scriptures of Vedas, this form of medicine dates back to over 5000 years. It has a holistic approach to address any disease condition. Health, as defined by Ayurveda is “...a balanced state of the senses, mind and spirit, all of which lead to health”. This is on par as defined by the World

Health Organization as “a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity”. Thus the understanding of health by Ayurveda applies to modern day scenario and its necessities.

There is also wide spread recognition and evaluation of the fact that a large number conventional western drugs of today evolved from medicinal plants. The ac-

ceptance of Ayurveda though comes with the need for evaluating plants for their therapeutic effects through modern techniques. The initial steps include the authentication of raw materials and selection of plant parts before the standardization to develop quality phytoextracts that are safe with potential benefits.

Raw material selection

With excessive demand from consumers for natural products, adulteration of the same has raised a lot of concern. Since it is the dried powdered form of plant materials that are supplied for further formulation development, there is a possibility of adulteration. A common example is the adulteration of *Cinnamomum cassia* with *Cinnamomum zeylanicum*,¹ although morphologically very similar; the two species vary in their coumarin content. Coumarin being well recognized for its blood thinning properties is thus a potential threat when given to normal subjects. Using taxonomic techniques that involve microscopy and DNA fingerprinting, this can be avoided.

Standardization

Standardization of plant material is a quality assurance program involving processes applied to herbal powders, extracts and dosage forms. These processes guarantee the minimum content of certain active ingredient(s) or marker compounds. This is an essential pre-requisite for plant based products since it delivers consistency in

dosage, predictability in therapeutic response and reduction in toxic components of biomass origin. Crude extracts contain varying concentrations of bioactive compounds that vary from one batch to the other due to various environmental conditions. It is essential to develop reproducible and robust processes of extraction in order to enrich the bioactive compounds and standardize the dosage. An example to elaborate this is as given below.

Ginkgo biloba is a well-known plant for improved cognition. Its active constituents include ginkgolide and a common allergen ginkgolic acid. Standardized extracts obtained through specific processes of extraction enrich the ginkgolide content from 0.06% in the crude extract to 3%, thus playing a vital role in reducing dosages. The process also reduces the allergen content from 2% to less than 6ppm.² This example is a standing example of improving both the safety and efficacy of plant extracts.

Standardization may also involve the selection of the appropriate plant parts at the correct season when bioactives are in higher quantities. A few examples such as *Cassia angustifolia*,³ *Tylophora indica*,⁴ *Capsicum frutescens*⁵ are tabulated below in Table 1.

Table 1: Chemical constitution of plants in different stages of growth

Plant name	Active constituent	Plant part	Bioactive content (%)
<i>Cassia angustifolia</i> ³	Sennosides	Vegetative	4.3
		Flowering	3.9
		Fruiting	2.63
		Sprouting leaf	7.1
<i>Tylophora indica</i> ⁴	Tylophorine	Pre-flowering leaves	0.45
		Flowering leaves	0.5
		Post-flowering	0.12

		leaves	
<i>Capsicum frutescens</i> ⁵	Capsaicin	28 days old fruit	0.07
		35 days old fruit	0.20
		42 days old fruit	0.43
		49 days old fruit	0.49

The lack of standardization may lead to the development of misleading extracts with several drawbacks. Primarily, the extract may contain variable or sub-optimal amounts of the active constituents which in turn is a compromise on safety and efficacy. Supplements may not even contain the active ingredients listed in the label. Of greater concern is that the extracts may contain synthetic compounds only to adhere to label requirements.

The need for standardization is thus very clear since it decides further the fate of the extract to deliver any benefits while ensuring safety.

Case studies from Ayurveda that have been scientifically validated

Turmeric: Turmeric is the most revered plant in Ayurveda, used as food supplement, spice and cosmetic ingredient throughout the world. Turmeric is rich in many phenolic compounds known as “Curcuminoids”, with Curcumin as the main active. In Ayurvedic medicine turmeric is well-documented for treatment of various respiratory conditions (e.g., asthma, bronchial hyperactivity and various allergies), liver disorders, poor appetite, rheumatism and influenza symptoms.⁶

Naturally present in the roots, the curcuminoids exist as curcumin, demethoxycurcumin and bisdemethoxycurcumin. They complement each other for various biological activities and in specific studies, one is found to have better activity than the other.^{7,8} However, the content of curcuminoids in the rhizomes of *Curcuma longa* is reported to be a maximum of only 3-4% by

weight.⁹ This would require consumption of higher dosages of crude turmeric for any therapeutic benefit.

With this understanding, the team of scientists at Sami-Sabinsa, while working on this traditional herb, Turmeric, derived and patented an optimized composition of Curcuminoids from rhizomes of turmeric to provide maximum antioxidant or bioprotectant activity. Known worldwide by its brand name, Curcumin C3 Complex[®] provides optimal antioxidant protection and maintains integrity of the biological system. The major components of Curcumin C3 Complex[®], are similar to their occurrence in nature, namely Curcumin, Demethoxycurcumin and Bisdemethoxycurcumin. In Curcumin C3 Complex[®], Curcumin makes up 75-81% of total Curcuminoids, DMC 15-19% and BDMC about 2.2-6.5%.¹⁰

With the earliest book on Curcumin published in 1993, today, Sabinsa’s Curcumin C3 Complex[®] proclaims of being the “**most extensively studied and clinically documented**” Curcuminoids brand available in the world. There are more than 80 research papers including 47 clinical studies published in peer-reviewed journals to date and documented in its most recent book “Curry powder to clinical significance”.⁶ These clinical studies have helped carve a unique place for Curcumin in the dietary supplement industry making Curcumin C3 Complex[®] “The Most Trusted brand” for over two decades.

Amla: Ayurveda’s own *Rasayana*, *Embllica officinalis*, is well recognized for its

rejuvenative and longevity properties. Conventionally, Amla extracts has been mainly promoted in and as a dietary supplement that is rich in ascorbic acid or with Vitamin C which has also been considered as the valid biomarker. This has been basis for its addition in several Ayurvedic formulations such as *Triphala* and *Chyanaprash*. With advances in modern science, the validity of ascorbic acid as a biomarker in Amla has been questioned. This has led to extensive research articles wherein Amla extract was supposedly characterized for Emblicanins A&B.

The research team at Sami-Sabinsa with its strong technical expertise, using the state-of-art facility analysed that Amla does not contain ascorbic acid in consistent amounts, and sometimes, only in trace quantities. Further, Emblicanins A&B were also incorrectly identified. High end analytical methodologies led to the discovery that β -Glucogallin and Mucic acid galates are the predominant active molecules in Amla, and that these molecules are significant contributors to the healthful effects of Amla.¹¹

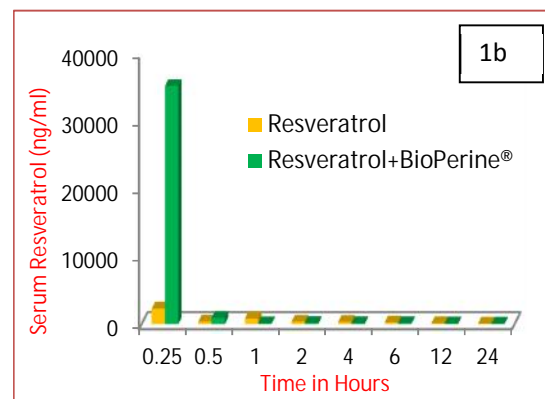
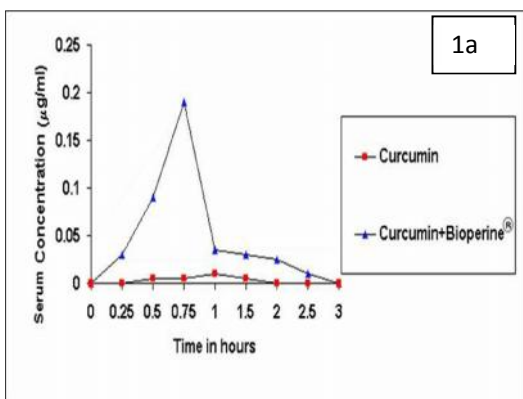
As a result Sami Labs isolated, characterized and commercialized the FIRST correctly standardized extract of the Amla fruits - **Saberry**¹. It is the result of efforts to prepare an authenticated Amla extract, standardized using a valid biomarker, S-

glucogallin. Saberry[®] has been extensively studied for various benefits and found to have a multi-faceted potential, thus confirming Ayurveda's recognition of Amla as a "Rasayana or Adaptogen."^{12,13}

Black Pepper: Black pepper is part of famous Ayurvedic formulations- *Trikatu* meaning "three acids". In Ayurveda *Trikatu* has been described as a major decoction useful in restoring imbalance of Kapha, Vata and Pitta.

Modern scientific studies have led to its use as a delivery system to encapsulate, protect and release bioactive and functional nutraceuticals in the food and pharmaceutical industries. **BioPerine**[®] the patented extract from Sabinsa obtained from black pepper fruits (*Piper nigrum*), has been used as a bioavailability enhancer for over 15 years. BioPerine[®] may be co-administered with various nutrients to enhance their bioavailability in both human and animal and has been found to enhance absorption of nutrients by at least 30%.

BioPerine[®], has been clinically tested with several nutrient groups including fat soluble vitamins (-carotene), water soluble vitamins (vitamin B₆, vitamin C), selenoamino acid (L(+)-Selenomethionine), Coenzyme Q₁₀ and shown to significantly enhance the bioavailability of supplemented nutrients through increased absorption. Herbal extracts such as curcumin and



resveratrol (Fig 1a and 1b) also absorbed better when co-administered with BioPerine®.^{14,15} It has been incorporated successfully into a number of formulation.

Figure 1a & b: Improved absorption of Curcumin and Resveratrol along with Piperine

Guggul: Native to India, the gum resin of *Commiphora mukul* has a long history of use in Ayurveda. Mentioned in the Vedas, detailed descriptions regarding the actions, uses, and indications as well as the varieties of guggul have been described in the Ayurvedic treatises Charaka Samhita, Sushruta Samhita and Vagbhata.

Gugulipid® is a patented standardized extract for guggulsterones Z & E from *Sabinia* obtained from the gum resin of

Commiphora mukul. This extract is evaluated for its cardiovascular support activity across the world in Institutes such as CDRI, CIPLA, Department of Veterans Affairs Medical Center (Arizona) and University of Pennsylvania.

A clinical study was carried out on 42 volunteers with elevated Lp(a) levels who were given 75mg of Gugulipid for 8 weeks. Gugulipid® lowered Lp(a) significantly.¹⁶ In another study on 30 volunteers for 12 weeks, 75mg Gugulipid lowered hs-CRP and MDA levels significantly (Fig 2).

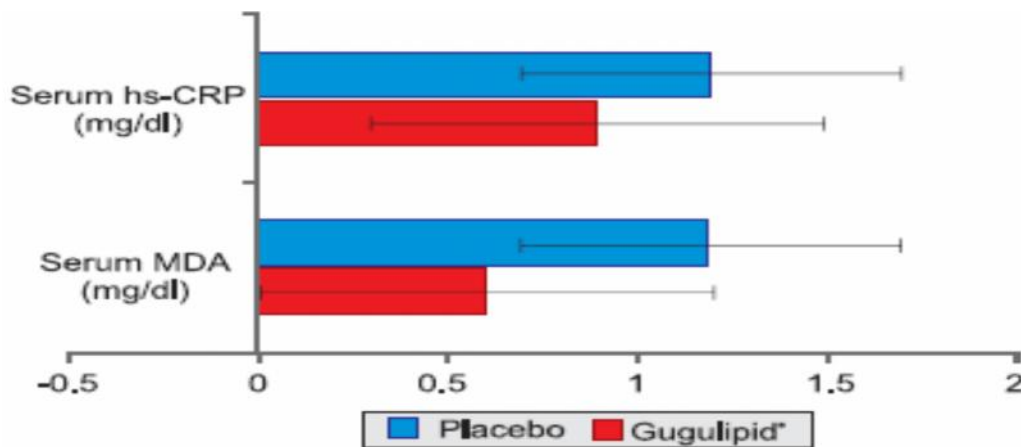


Figure 2: Reduction in hs-CRP and MDA levels with Gugulipid®

Boswellic acids: The gum resin exudates of *Boswellia serrata*, known in the vernacular as “Salai guggal”, have been used in the Ayurvedic system of medicine in the management of several inflammatory disorders. Its use is implicated in a range of disorders including cardiovascular disease, fever, jaundice, asthma, cough, diarrhoea etc.¹⁷

The major use of *Boswellia serrata* in contemporary medicine is as an anti-arthritis and anti-inflammatory agent. The anti-

inflammatory properties of the gum resin attributes to the presence of Boswellic acids. Some of the identified and characterized BA include -Boswellic Acid, 3-O-Acetyl- -Boswellic Acid, 11-Keto- -Boswellic Acid and 3-O-Acetyl-11-keto- -Boswellic Acid. Of these, 3-O-Acetyl-11-keto- -boswellic acid (AKBBA) is reported to be the most potent anti-inflammatory molecule.

Boswellin® is obtained from the gum exudates of *Boswellia serrata* trees standardized for identified boswellic acids. The Science – Chemistry and Mechanism of

Boswellia serrata Gum has been published in more than one book by Sabinsa. Boswellin[®] is clinically proven safe and effective in the management of several inflammatory disorders.

Coleus: The roots of *Coleus forskohlii* have a long history of food use in India in the form of pickle / condiment. Historically, it has been used to treat heart diseases, respiratory disorders, insomnia, asthma, bronchitis, intestinal disorders, burning sensation, constipation and skin diseases. ForsLean[®], is manufactured by Sabinsa by a proprietary process. It is a standardized extract from the roots of the *Coleus forskohlii* plant, the only known plant source of the Forskolin. The introduction of Cole-

us into the global market for weight management and to enrich Forskolin content from 1% to 99% in the extract is a pioneer work of Sabinsa. There have been several clinical studies with ForsLean[®] that have been carried out globally to evaluate its role in promoting lean body mass. These studies have paved way for its approval by the Korean FDA as a weight management ingredient.

In one open field study, 6 overweight women subjects were given 500 mg ForsLean[®] corresponding to 50 mg forskolin/day for 8 weeks. A significant reduction in mean weight and mean body fat and an improved lean body mass was observed (Fig 3).¹⁸

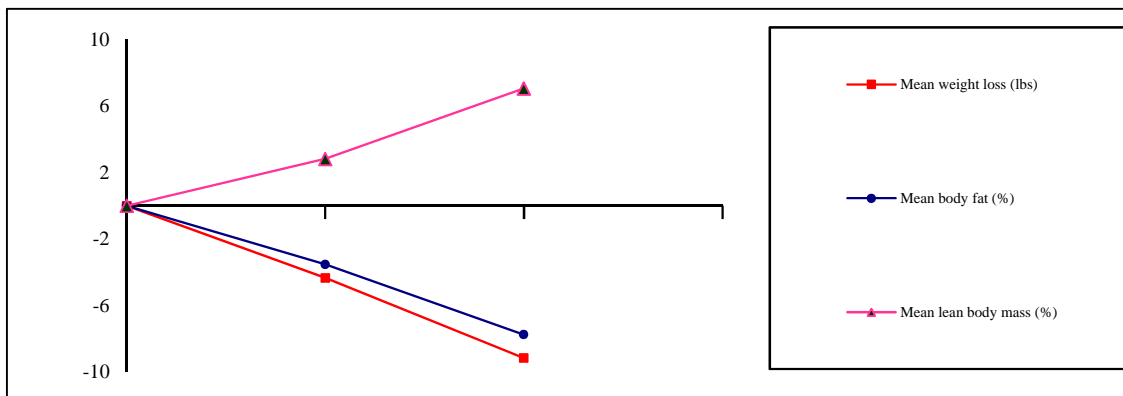


Figure 3: Effects of ForsLean[®] on Body Weight, Body Fat and Lean Body Mass

Ocufors[®] Eye Drops for Glaucoma containing 1% Forskolin is the first natural drug to go through full-fledged clinical documentation to obtain a drug approval. Patented across the globe, it is found to reduce intraocular pressure as evaluated through a clinical study.

Garcinia cambogia: Belonging to the family Clusiaceae, it is a small, pumpkin-shaped fruit, also called as Malabar tamarind. Mentioned in the verses of Charaka Samhita, it is well recognized for its property to rejuvenate and refresh the body.

Citrin[®] and GarCitrin[®] are natural weight loss aids from the fruits of *Garcinia cambogia*, and have been demonstrated for the same in pre-clinical and clinical studies. Its active constituent (-) Hydroxy citric Acid has been evaluated for its potential role in weight loss. A patented and GRAS certified ingredient, GarCitrin[®] has also won the Thomas Alva Edison Patent award for Sabinsa.

Hydroxycitric acid (HCA) has been shown to be a potent linear competitive inhibitor of adenosine triphosphate (ATP) citrate lyase enzyme. This leads to both the reduction of fatty acids synthesis and lipogenesis. HCA also facilitates the oxidation pro-

cess of fatty acid, which meets the energy requirements of the body. This is by indirect activation of L-carnitine acyltransferase. It also increases the satiety.¹⁹

The efficacy of 1500 mg of the calcium salt of HCA (750 mg of pure HCA) and 300 mcg of elemental chromium per day for body weight loss in overweight human subjects was evaluated. This open field, physician controlled eight week clinical study was evaluated in 55 overweight subjects of both genders with a body mass index of $>25 \text{ kg/m}^2$ and $<45 \text{ kg/m}^2$. Along with a significant reduction in body weight, the blood levels of triglycerides (TG), VLDL and LDL were significantly lowered.²⁰

Vijaysar: Well documented in the Ayurveda, the bark of *Pterocarpus marsupium* has been widely used to manage elevated blood sugar levels. Since ancient times, Ayurvedacharyas used blocks or pieces of *Pterocarpus* or “**Vijaysar**” to control diabetes. Pieces were soaked in water over-

night, sieved and taken by diabetic patients. This was further improved by preparing tumblers carved from the wood of *P. marsupium* in which water was stored overnight.

Pterodin™ WS is obtained from the heartwood of *Pterocarpus marsupium* and is standardized for C-glycosides. C-glycosides from *Pterocarpus marsupium* have been found to be safe and effective SGLT2 inhibitors as evaluated through clinical studies for their blood sugar management. Inhibition of Sodium Glucose Co-Transporters (SGLT2) is a novel therapeutic strategy to control diabetes.

In a flexible dose open trial in 4 centers in India, increasing doses of **2g, 3g and 4g** (4 weeks each) of **Vijaysar extract** were given to Type 2 diabetes patients and were analyzed for their blood glucose levels (fasting and post-prandial). Fasting and postprandial blood glucose levels were observed to be **controlled in 12 weeks** (Fig 4).²¹

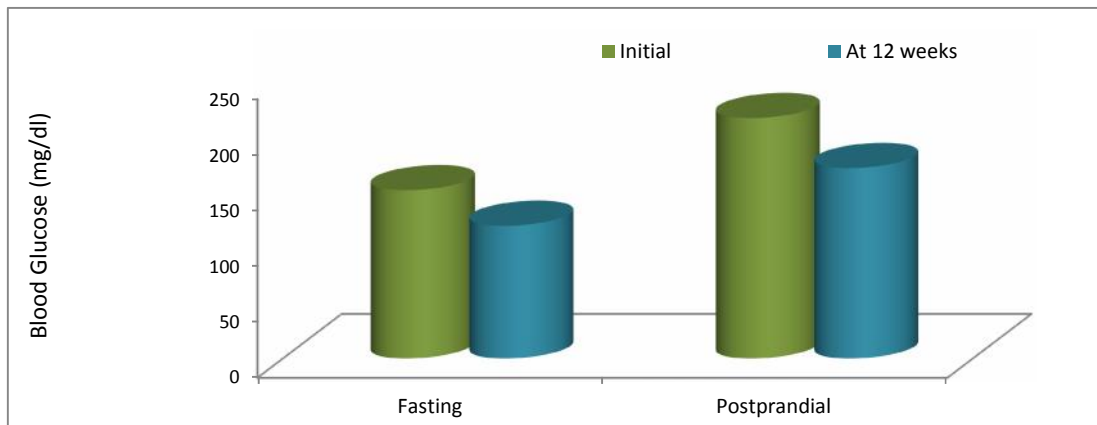


Figure 4: Fasting and postprandial blood glucose levels

CONCLUSION:

The above few examples justify the need for standardization of plant extracts mentioned in the Ayurveda to deliver quality phytoextracts for potential benefits. The journey of Ayurveda, from being only crude herbal extracts to standardized phyto-extracts, has seen success and found due recognition across the globe. However,

this is limited to only a few extracts and the list could well be extended with the involvement of more from the scientific fraternity carrying out relevant projects.

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CORRESPONDENCE AUTHOR

Dr. Vaidyanathan Priti

Senior Manager

Sami Labs Limited, # 19/1, 19/2, I Main, II Phase, Peenya Industrial Area, Bangalore – 560 058, Karnataka, India

Email: prtipv@samilabs.com

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