

A patented product specifically developed to maintain healthy blood sugar levels

.....
Produced from the seeds of the edible plant *Syzygium cumini* (L.) Skeels

.....
Pharmacological and Clinical data support its efficacy

.....
A safe product, devoid of any side effect

Madeglucyl[®]

Syzygium cumini fruits

■ **Hyperglycemia** is recognized to be the central feature of all the unbalances in the metabolism of carbohydrates, lipids, ketones and amino acids.¹ The most diffused pathological condition characterized by stable hyperglycemia is known today as **type 2 diabetes** (accounting for about 90% of all diabetes cases) which is considered an epidemic disease, in particular in Western Countries where the incidence in the population is estimated to range from 2 up to 4%.²

Type 2 diabetes is usually preceded for years by an abnormal condition called **impaired glucose tolerance** (IGT) characterized by plasma glucose levels, 2 hours after an oral glucose challenge, above normal (>140 mg/dL) but not so high as in diabetes (>200 mg/dL). Several characteristics in the population have been recognized to be associated with a greater risk of progression from IGT to type 2 diabetes. Among these, an impaired insulin secretion, insulin resistance, obesity and age.³

Physical exercise and appropriate dietary measures are usually suggested as a first line approach in pre-pathological hyperglycemic conditions. In the last years, targeted dietary regimens are also including **natural products** that can be of help in maintaining **healthy blood sugar levels**. In particular, some plants, traditionally used for their hypoglycemic effects, have been considered for this specific issue. Among these plants, a particular attention has been devoted by Indena to those used in the dietary habits.

A natural way to maintain healthy blood sugar levels

Madeglucyl[®] is a patented botanical derivative from the seeds of *Syzygium cumini* (L.) Skeels, an **edible plant** named also *Eugenia jambolana* Lam.

Ever since, this plant has been used both in Europe and in other countries (India and Southeast Asia) in folk medicine for its **anti-hyperglycemic properties**. Madeglucyl[®] is produced from the seeds of the plant using solvents admitted by food law (Directive 88/344/EC) and has been characterized by means of two different assays: content of ellagic acid by HPLC (~2% after hydrolysis) and bio-assay (not less than 20% glycemia reduction in glucose loaded rats).

Toxicological and pharmacological data show that Madeglucyl[®] is devoid of any side effect and can provide a support in maintaining **normal sugar levels** in several experimental conditions.

Madeglucyl[®] had its efficacy proven by **clinical data** obtained from studies in Madagascar, Germany and USA, where it demonstrated a good tolerability and a significant effect **already 15 days** after starting the treatment.

Proven efficacy

The efficacy of Madeglucyl® was verified at dosages ranging from 1 to 6 g in clinical trials performed in Madagascar, Germany and USA.⁴⁻¹⁰ The overall figure of the effects of Madeglucyl® can be summarized as follow:

- Reduction of glycemia in healthy volunteers (-20% at glucose peak time 60 min after oral glucose load, chart 1)
- Reduction of glycemia (-49%, after 90 days) in subjects suffering from type 2 diabetes (chart 2)
- No hypoglycemic effects in healthy subjects
- Absence of hypoglycemia as a side effect in patients affected by type 2 diabetes
- Good tolerability in all the treated subjects even at the highest dosages

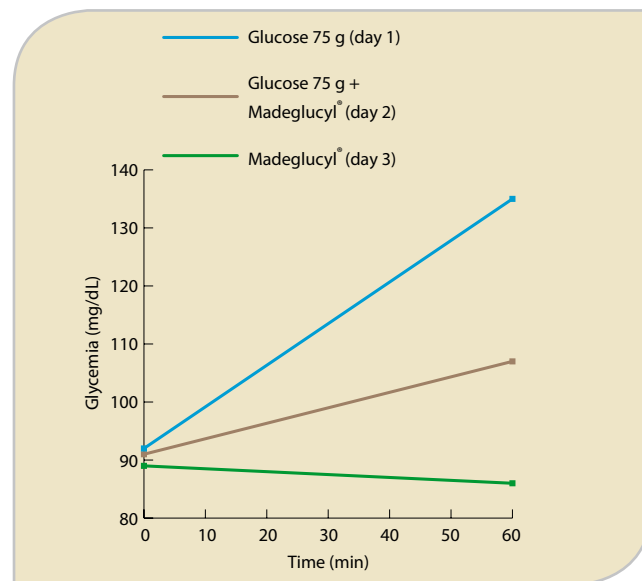


Chart 1: effects of Madeglucyl® on blood glucose levels in healthy volunteers. The test was performed in three subsequent days. On day 1, the fasting subjects received a solution containing 75 g of glucose p.o., according to the National Diabetes Data group. On day 2, same solution was administered and 3 g of Madeglucyl®. On day 3, only Madeglucyl® (3 g) was given.

Toxicology

Acute, sub-acute toxicological studies in rodents and chronic studies in rodents and rabbits demonstrated the safety of Madeglucyl®. All the studies of teratogenesis performed in rodents and rabbits were also certifying the total absence of negative effects.¹¹

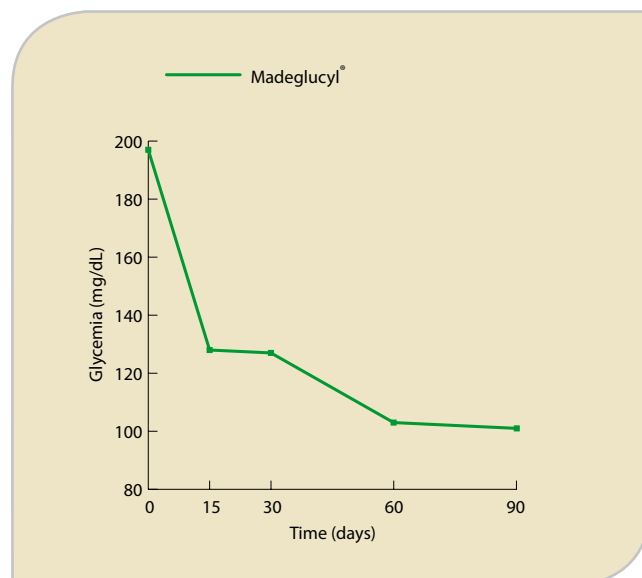


Chart 2: effects of Madeglucyl® in patients affected by type 2 diabetes. Madeglucyl® was administered p.o., at dosages up to 6 g/day (average dosages ranging from 2 to 3 g/day), for 90 days. Blood glucose levels were measured at days 0, 15, 30, 60 and 90 from the beginning of the treatment.

Pharmacology

The oral hypoglycemic and antidiabetic activity of Madeglucyl® has been observed in dosages ranging from 50 to 500 mg/kg in several models of hyperglycemia such as:¹²⁻¹⁵

- Glucose tolerance test in rabbits (chart 3), mice and rats (reduction of glycemia after glucose load >20%, comparable with glybutamide and metformin)
- Experimental diabetes induced by alloxan in rats (chart 4) and mice (reduction of glycemia >40% versus control)
- Genetically obese and diabetic DB/DB mice (reduction of glycemia >40% versus control)
- Spontaneously diabetic sand rats (normalization of glycemia and prolongation of life)

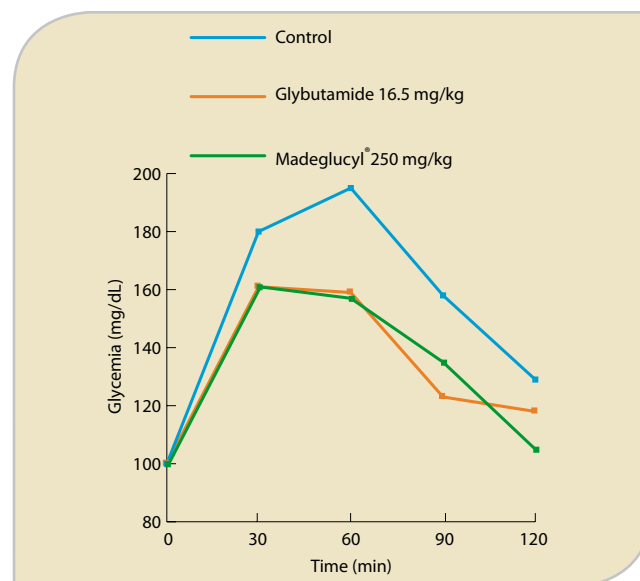


Chart 3: effects of Madeglucyl® on blood glucose levels in rabbits, receiving (at time 0) 1 g/kg of glucose and 250 mg/kg of Madeglucyl® or 16.5 mg/kg of glybutamide by oral route. A group of animals was used as a control. Blood samples were collected at 30 min intervals for two hours.

Botany

Syzygium cumini (L.) Skeels (Syn. *Eugenia jambolana* Lam.) Myrtaceae family

A tree, usually of considerable size, attaining 30 m in height and 3.6 m in girth.

Bark pale brown, slightly rough on old stems with shallow depressions, exfoliating in woody scales;

leaves, lanceolate, elliptic-oblong or broadly ovate-elliptic, 7.5 - 15 cm x 3.8 - 6.3 cm., coriaceous, smooth, and shining above, with numerous close parallel fine secondary nerves uniting to form an intramarginal vein;

flowers greenish white, fragrant, sessile, arranged in trichotomous panicles 3.8 - 10 cm long; calyx-tube 2.5 - 5 cm long, turbinate; limb truncate, or obscurely 4-lobed, petals united into a thin membranous calyptra;

fruit ellipsoid or oblong, up to 2.5 cm long, black with pinkish juicy pulp, crowned with the truncate calyx-limb;

seed single, shaped like the fruit, 1 - 2 cm long, or 2 - 5 seeds together into a mass tightly compressed, within a leathery coat.^{16,17}

The tree is native in India, Myanmar, Ceylon and the Andaman Islands; commonly cultivated in tropical areas of the world as ornamental plant or for its juicy fruits, often eaten raw or used for tarts, sauces and jam.¹⁸

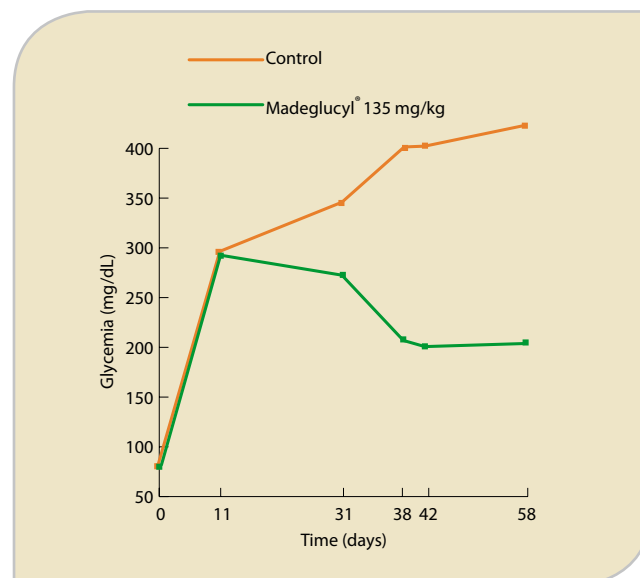


Chart 4: effects of Madeglucyl® in experimental diabetes. Wistar male rats were treated with 150 mg/kg of alloxan (day 0). After 11 days, the rats received 135 mg/kg of Madeglucyl™ for 48 days. Blood glucose levels were measured at days 11, 31, 38, 42 and 58 after the administration of alloxan.

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