

THE GARCINIA CAMBOGIA IN PHYTOTREATMENT OF OBESITY: ACTIVITIES OF THE HYDROXYCITRIC ACID

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Abstract

The objective of our work has been the identification in the bark of *Garcinia cambogia* (GC) of the HCA that has proven effective in blocking weight increase. The Hydroxycitric Acid (HCA) is a present alimentary acid in some varieties of tropical fruits, between which the *Garcinia cambogia* Desr. Its effect on the organism is that one to block to the activity of ATP-citrate lyase in charge of the transformation of alimentary sugars in fat people of reservoir for the body. The hydroxycitric acid has been isolated from the dried peels of GC after shredding and Soxhlet extraction with distilled water for several hours. After repeated treatments with alcohol on the watery residual and solvent evaporation, a residual light yellow has been obtained that it has undergone to several chromatographic analysis. The use of the chromatographic methods is useful for the purposes of evaluating a drug like phytocomplex allowing to know the nature of the active principles in it contained. The characterization of the phytocomplex thus obtained allows the location of eventual sophistications or adulterations of the vegetable drugs in products trade them monocomponent even if are not known the constituent assets or the markers of the same one. Herbal medicines only composed from GC are proved to be effective in the treatment of obesity, without to introduce side effects during the period of therapy. Undesirable reactions have been found, instead, after administration of products obtained with adding to the GC of other phytocomplexes

Keywords: Hydroxycitric acid, *Garcinia cambogia*, TLC and HPLC, Pharmacological activity

Introduction:

The obesity represents a social problem of immense entity in the whose resolution comes been involved on alternation of successes and

failures food industries, pharmaceuticals and cosmetic ones. Multiple factors contribute to establishment of the obesity that can depend is from hereditary factors that psychological and economic acclimatize them. It is spoken about obesity when the index of body mass of an individual ($BMI = \text{body mass index} = \frac{\text{body weight}}{\text{height}^2} = \text{Kg/m}^2$) exceeds the value of 30. Beyond determining a showy modification of the order and the aesthetic body, the obesity involves various disturbs to second of its gravity. Between more you attend are acne, breathlessness, difficulty of movement, alterations of the menstrual cycle, crisis of apnea during the sleep and premature atherosclerosis. To it numerous complications are correlated: cardiovascular hypertension, diabetes, diseases (angina, myocardial infarct, ictus) that without a doubt are feared (Jebb SA,1999), moreover premature arthrosis, alterations of the hormonal picture, hirsutism, amenorrhoea in the women, reduction or expectant loss of the self esteem, anxious syndromes, disturbs of the sleep.

The treatment of the over weight and the obesity involves mainly a aimed participation to educate the subject on one correct feeding: irregular and hasty meals, carbohydrate meal outside rich, alcoholic drinks are the root causes of rebelling of the obesity; if to they one joins to a sedentary activity and a stressed way of life, phrenetic, little relaxing, the typical picture of the subject is obtained over weight (Martínez Vizcaíno V. et al, 2013)

The pharmacological therapy becomes an indispensable treatment when to the obesity is associated more serious pathologies to cargo of the cardiovascular system, of the glycidic and lipidic metabolism, let alone of the respiratory and locomotor apparatus. The treatment is dietetic that pharmacological they must be you follow yourself under tightened medical control from the moment that long times preview much in order to obtain turn out to you obvious and therefore the patients who must submit to precise timetables in order to assume meal and pills, become irritable, disheartened and often they abandon the therapies or to resolve the problem drastically, undergoing itself to surgical therapy, or they accept of good degree of sottoporsi to fitoterapici remedies (Sindler BH, 2001).

All the people since the ancient times have used a variety of plants or materials derive from the plants for the prevention and the treatment to you of the diseases. The test of the benefits therapeutic effects of these medicinal grass is demonstrated from their continued use. The development of modern chemistry has allowed to the isolation of substances chemistries from medicinal grass used like drugs or materials of departure for the synthesis of many currently used important drugs. The medicinal grass has carried out an important role in the development of the modern medicine and continues wide to being used in their shape originates them.

Garcinia cambogia Desr, known also like “tamarindo malabar”, is a plant pertaining to the family of the Guttifereae that comprises numerous species between trees, shrubs, lianas and grass between which some notes for their medicinal property. The yellow-orange fruit color has the shape of pumpkin with thin skin and deep vertical sections that form lobes; the natural habitat is represented from the warm zones of Asia, South Africa and Polynesia and is known for its alimentary value being commonly used like spice or conserving above all of the fish.

In the traditional medicine the fruit of the *Garcinia* finds employment is for the problem solving to level of the stomach and of the intestine, it is like oral antiseptic in the mouthwashes. Such property astringents and antiseptic have been found in the peel of the fruit that comes dried and used also in order to prepare infusions and decoctions. In 1965 it has been isolated from the peel of the *Garcinia* the active principle, the hydroxycitric acid, an hydroxy acid with two atoms of *C for which four isomers are possible (LewisYS,1965) of which two they are present in the fruit. Into their great instability they are transformed fastly in the correspondents lactones (Fig 1).

The HCA carries out an important role in the management of the body weight and the appetite: it inhibits the production of hepatic enzyme ATP citrate-lyase that transforms carbohydrates does not consume in fat limiting in such a way the formation of fat person of warehouse, harmful because it is accumulated mainly in the subcutaneous adipose woven one and he is the main one in charge of the increase of the body weight. It stimulates moreover the hepatic synthesis of glycogen beginning from the glucose, with increase of the warehouse of this sugar of reservoir in the liver and muscles (Jena BS et al.,2002)

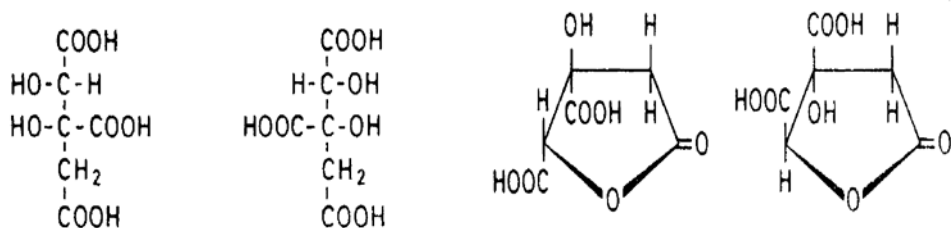


FIG.1 (-)-hydroxycitric acid (+)-hydroxycitric acid dexter lactone
laevo lactone

Experimental part:

Potassium hydroxycitrate tribasic monohydrate purchased from (Sigma-Aldrich (Milan, Italy) used as a reference Metavanadato purchased from Todini sodium and Co Spa (Monza, Italy) 5x20cm cellulose plates and all solvents for thin-layer chromatography and HPLC

grade Solvents were purchased from Merck (Darmstadt, Germany) HPLC apparatus: Sunicom Oy (Helsinki, Finland) connected with UV/VIS detector with variable wavelength 500 Model equipped with a degasser ERC3TT. The Ultracarb 5 μ ODS column (20) 250 x 4.60 mm was purchased from Waters S.p.A (Milan, Italy)

The HCA has been isolated from the dried peels of *Garcinia cambogia* after shredding and extraction in Soxhlet for various hours with distilled water. After concentration to small volume, vacuum packed by means of rotovapor, the watery solution has been added of alcohol in order to eliminate the pectic substances and alkalized with KOH solution 0.1 N. A dark viscous liquid has been obtained that as a result of settling has introduced two is made. After elimination of the supernatant the inferior layer that was introduced like oily liquid, containing the salt of acid, has been washed in separatory funnel with alcohol to 60% various times, obtaining after repeated treatments and removal of the solvent a residual yellow pale that has been dissolved in distilled water and subordinate to chromatographic analyses.

The identification has been executed by means of chromatography on thin layer using plates of cellulose 5x2cm Merck and Potassium hydroxycitrate tribasic monohydrate like reference. They have been employed following eluent systems:

- n-Butanol/acetic acid/water (4: 1: 5)
- n-Butanol/formic acid/water (4: 1: 5)
- Ethyl ether/formic acid/water (10: 1: 5)
- n-propanol/ammonia/water (6: 3: 1)

A solution to 3% of sodium metavanadate, evidenced on the plate, after heating in stove to 70°C, 4 spots with values of R_f comprised between 0,2 and 0,5; the relative spot to hydroxycitric acid with R_f 0,34 it was colored in yellow orange while the spot with R_f 0,46, relative to its lactone was colored in yellow.

The free hydroxycitric acid has a survival much limiting and during the processes of evaporation and concentration it stretches to form the lactone; it knows them of Ca and of K of acid they have, instead, they introduce one good stability. In order to confirm the presence of hydroxycitric acid, 10 μ L watery solution of the residual one 5 μ ODS (20) 250 x 460 mm have been injected in an apparatus HPLC using an Ultracarb column 5 m ODS (20) 250 x 460 mm and like eluent system a solution of sulfuric acid 10 mM with flow 0,7ml/sec under isocratic conditions and determining the absorbance to 214 nm

As the elevated peak with R_t= 4,7 appears more in Fig 2 identifies hydroxycitric acid like main member of the extract, followed to short time

from a peak more low relative to the lactone, while other acids, in smaller concentration are present with Rt higher .

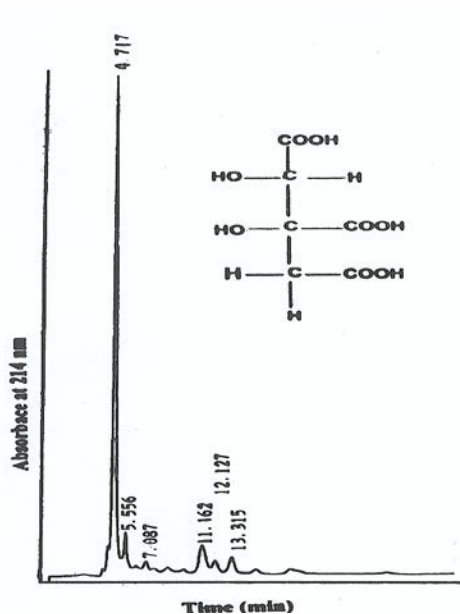


FIG. 2 HPLC identification of hydroxycitric acid

Hydroxycitric acid activity:

The process of appraisal of the medicinal grass potentially equipped of therapeutic effectiveness is much complex, and strategy of search for the guarantee is the necessity to define with attention one of sure and effective erboristic products. While it is simple to extract from a plant principles with pharmacological property to use as drugs it is met many difficulties in the preparation of an extract standardized vegetable that it supplies coherent pharmacological activity. In the extract total of the plant the various active principles contribute in synergistical way to the pharmacological action, while numerous studies, sufficient are brought back in order to suggest that the active principles isolate to the pure state, are in a position to producing pharmacological effects that meaning fully defer from that one of all the plants.

Recently many studies on animals and humans they have been you execute employing extracted hydroxycitric acid from the *Garcinia cambogia* Desr in order to evidence its ability to reduce the body weight (Ramos RR, et al. 1995; Soni MG, et al 2004; Mohammad Asgharet et al. 2007).T he primary mechanism of action of HCA seems to be correlated to its ability to act like competitive inhibitor of the ATP-citrate enzyme lyase, that it catalyzes the conversion of citrate and CoA to oxalacetate and Acetil

Coenzyme A (acetyl-CoA), primary construction of fat acid blocks and the synthesis of the cholesterol. The demolition of sugars, proteins and the ingested fats happens in the mitochondria through the cycle of Krebs with energy production through the respiratory chain. When the sugar, food ingestion in particular, is in excess, a part of the citrate one where exits in the cytoplasm to work of the enzyme citrate-lyase, gives origin to fat acids, to the cholesterol and consequently to an increase of body fat person, that it comes deposited in the adipose tissue. The hydroxycitric acid strongly limits the activity of the enzyme citrate-lyase blocking drastically this process of storing under fat person shape, favouring the complete demolition of the foods with energy production. The positive result to the ends of prevention of the obesity is the consequent sense of satiety.

The discovery of the powerful inhibition of the enzyme citrate lyase from part of hydroxycitric acid it supplies a precious instrument for the study of the metabolic role of the enzyme citrate-lyase. In the course of the years, studies in vitro and vivo they have demonstrated that the hydroxycitric acid prevents from the origin the synthesis of fat acids and the lipogenesis reducing the transformation of sugars in fats in the cell and accelerating of the elimination (Watson JA et al ,1969)

Hackenschmid J.(1972) demonstrated that the hydroxycitric acid is a positive effect of acetylCoA-carboxylase acting like inhibitor of lipogenesis if the acetylCoA cytoplasmic is produced from the action of the enzyme citrate-lyase, but could only activate the fat acid synthesis as an example if an alternative were available source of acetylCoA, the acetate.

Cheema-Dhadli S.(1973) experiencing the inhibiting power is of the free HCA lactone found that both introduced inhibition that but was revealed greater for free hydroxycitric acid.

Beynen AC and Geelen MJ (1982) observed the inhibition of the synthesis of fat acids coming from glucose by means of (-)- HCA are in the hepatocita one of isolated rat and perfused, it is in the omogenate one of this organ. This effect was attributed to the activation of the acetylCoA-carboxylase, in analogy with the tricarboxylate enzyme.

Hood et al.(1985) demonstrated that the hydroxycitric acid reduced the fat acid synthesis in lactate presence and glucose is in tissue the adipose bovine that in the adipose tissue one of the rat as a result of the conversion of the lactate one in fat acid through the cytrate one. In the cells of rat liver dealt with hydroxycitric acid, in fact, had been noticed a lessening in the formation of phospholipids and triglycerides in presence of lactate

Vicario C. and Medina JM. (1991) also have brought back the inhibition of the lipogenesis in lactate presence of in the brain of rat by means of HCA, reduction of the biosynthesis of triglycerides, phospholipids,

cholesterol and free fat acids in isolated cells of liver from normal and hyperlipidemic rats.

Heymsfield SB. et al. (1998) study in blind double quantity for 12 weeks on subject males and females of age comprised between 18-65 have experienced the activity of HCA by means of one years with MBI between 27-38 Kg/m².

They were subdivided in two groups of 66 and 69: to first it is been administred 1,5 g of HCA to the day, while to second the placebo, prescribing to both one rich low calorie fiber diet. Only 42 persons in the first group and 42 persons of second group carried to term the experiment showing all a meaningful loss of weight, but other meaningful differences were not evidenced, for which the experimentation it was not judged meaningful to the ends of the treatment of the obesity.

Badmaev V et al. (1999) refuted turns out of Heymsfield, charging the insufficient significance of the result is to the low concentration of administered HCA, is to the rich fiber diet: such combination had reduced the HCA absorption and therefore its bioavailability in citosol of the cells target with consequent lacked inhibition the synthesis of lipids. The bioavailability of the HCA was diminished from the presence of calcium salts used in order to stabilize the molecule, while a greater effect obtained with one rich diet in simple carbohydrates. It has been moreover observed a greater bioavailability of the *Garcinia cambogia* when it comes assumed to empty stomach.

Studies executed from Ohia SE. and coll (2002) they have evidenced the ability to the HAC to increase from cortex cerebral of rats the release and the bioavailability of the serotonin an important neurotransmitter been involved in the control of the appetite. It could be thought to an other mechanism of action that is involved the HAC with an increase of the levels of serotonin in the brain that would involve one reduction of appetite the consequent lessening of the body weight. The ability to the HAC to act on the body weight would be determined from the effects arranges on the metabolic ways and the release of serotonin.

Conclusion

Many drugs modern they have been synthetized as a result of the acquired knowledge from the studies of action mechanisms active principles isolate from the medicinal plants. The medicinal grass has carried out an important role in the development of the modern medicine and currently consumption of various grass products is assisted to a return to the traditional medicine with an crescent in order to prevent/cure pathologies. The herbal products are considered from the greater part of the persons not harmful because natural; they can be assumed for along period of time and are

preferred regarding synthesis drugs consider harmful for their effects collaterals. Therefore the appraisal of the emergency of the used medicinal plants as phytotherapeutic products it is assuming a remarkable importance and it demands from part of the investigators a great effort for research purposes of suitable chemical- toxicological methods in order to guarantee the safety of such products

The extracts of *Garcinia cambogia* have been subordinates to deepened chemical studies / pharmacological are in vitro that in vivo, it is on animals that human beings. (.Li Oon Chuah, et al,2012) The scientific base of departure turns out sufficiently rich and very articulated such from being able easy to comprise the mechanism of action of the active principle of the plant, hydroxycitric acid, and to optimize therefore its use. They are not known effects collaterals and/or adverse reactions to the extracts trade them of *Garcinia cambogia*, such from being able to limit one they use. From the present data in literature it turns out obvious that a use rations them of *Garcinia cambogia* in scientifically valid a dietotherapeutic outline, turns out effective in the cure of the obesity (Antiwal Meera et al, 2013).

The obesity today it comes considered a world-wide problem of public health with a resource to cures alternative that are based mainly on phytotherapeutic formulations. The crescent ask of herbal extracts can easy be comprised being considers produced natural, than they do not cause to effects collaterals or damages for the health. Recent studies but have demonstrated the presence of synthetic substances not declared in label, namely adulterating substances, in the composition of these products that are cause of effects much sometimes serious collaterals.

The brought back cases of adulteration in literature refer to the use of anorexic, substances mainly, benzodiazepine and antidepressants, diuretic, that they are responsible of reactions to cargo of the cardiovascular apparatus, of the digesting apparatus, of the central nervous system, of the liver and other organs between which kidneys, thyroid and pancreas (Leandro M. de Carvalho et al. 2011)

Also the extracts of *Garcinia Cambogia* in various preparations trade are added them with other species vegetables, mineral substances that acting sinergically upgrade the slimming action [Girola M et al. 1996; Rothacker DQ,et al. 1997; Vasques CAR et al. 2008].The association with silvestre *Gymnema*, gymnemic rich responsible acid plant of the inhibition of the absorption of sugars to intestine (Preuss HG et al., 2004) turns out particularly useful when it needs a dietotherapeutic treatment that drastically reduces the coming from caloric contribution from the metabolism of the fat and the glycid, but its assumption is advisable to the single healthy adult subjects. In fact it could bring serious damages if administred to patients who suffer from diabetes of type 2 in pharmacological treatment, because

Garcinia cambogia is in a position to blocking carbohydrates and therefore to lower the level of sugars in the blood. Reactions of allergic type, hepatic toxicity, disturb renal, states got depressed, are from attributing to the adulterating substances associate you to the extracts of *Garcinia*, therefore as it disturbs of gastro intestinal are from attributing to an excessive dosage, advanced to the dose of 500mg/die. The signal of the adverse reactions caused from the presence of substances adulterating in phytotherapeutic formulations has rendered the study of new methodologies necessary in order to reveal such substances. The resource to methodologies analytic which the chromatographic techniques becomes important is from a clinical point of view that toxicological and in particular the HPLC, diffused technical consolidating into routine analysis all over the world, is fundamental for the identification and quantization of the substances adulterating present in a phytocomplex

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