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A REVIEW ON “GARCINIA CAMBOGIA – A WEIGHT CONTROLLING AGENT”.

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ABSTRACT

Obesity is a major problem in the affluent societies of developing and developed world and the Health Risks associated with the obesity are

Diabetes mellitus, Heart disease, High b.p., etc.

WHO report –Globally with more than 1 billion adults overweight - at least 300 million of them clinically obese.

Main cause of obesity is a person consumes more calories from food than he or she burns.

Now a days herbal drug are used because of its lesser side effects as compared to synthetic drugs.

This review provides complete information about the herbal drug *Garcinia cambogia* and its action in controlling weight.

The *Garcinia* fruit is a rich source of hydroxycitric acid (HCA), the active agent that aids in weight loss by inhibiting fat production and suppressing appetite.

Garcinia cambogia extract is quickly becoming a popular ingredient in many weight loss supplements.

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Key Words : obesity, herbal medicines, *Garcinia cambogia*, ayurvedic treatment, hydroxycitric acid (HCA), antiobesity drugs.

INTRODUCTION

The fruit of *Garcinia cambogia* has been traditionally used in food preparation and cooking. In Ayurveda, it is said that sour flavors such as those from *Garcinia* activate digestion. *Garcinia* is considered to make foods more filling and satisfying and has been used routinely for many centuries with no toxicity. *Garcinia* and its active ingredient, HCA (hydroxycitric acid) have been extensively studied for over thirty years and found to be effective in inhibiting lipogenesis, suppressing appetite, and encouraging weight-loss in laboratory animals.

ORIGIN

Garcinia cambogia, an exotic fruit grown in South India, has been used to impart a distinctive sour flavour to Indian cooking. It is commonly found in the evergreen and shola forests of Western Ghats in India up to 6,000 ft. high.

PHARMACOGNOSTIC STUDY [2,3]

Botanical Name: *Garcinia cambogia*

Family: Guttiferae

Plant Parts Used: Fruit rind

Common/Trade Names: Vilati – Amla

Sanskrit and Hindi Names: [4] Vrikshamla

Other Common Names of *Garcinia Cambogia*: Brindle berry, brindall berry, *garcinia*, malabar tamarind, gambooge, gorikapuli, uppagi, *garcinia kola*, mangosteen oil tree.

Habitat: India and South East Asia.

Description: *Garcinia cambogia* (Family: Guttiferae) is a small or medium sized tree with a rounded crown and horizontal or drooping branches. The fruits have six to eight seeds surrounded by a succulent aril and the tree is distributed commonly in the ever green forests of western Ghats, from Konkan southward to Travancore and in the forests of Nilgiris up to an altitude of 6000 ft. It flowers during the hot season and fruits ripen during the rainy season. The fruit is harvested, dried and ground into a powder.

Garcinia cambogia extract is the calcium salt of hydroxycitric acid (Both 50% and 60% hydroxycitric acids are available), which is obtained from water extract of *Garcinia cambogia* fruit.

It is non-toxic, tasteless, odorless powder and found to be very effective herbal medicine for controlling obesity and cholesterol by inhibiting lipogenesis in our body. It is a well established fat burning agent all over the world.

Chemical Constituents: [5] The plant contains various chemical constituents such as Xanthenes, Benzophenones, Garcinol and plant acids like (-) Hydroxycitric Acid, Maleic acid, Citric acid.

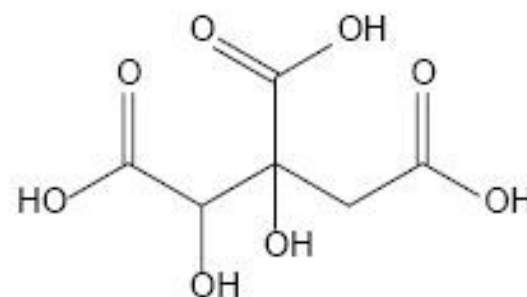
HCA is naturally occurring fruit acid found in the outer layer covering of the fruits of *Garcinia cambogia*.

HCA is highly unstable and therefore extracted as a salt of preferably as calcium or potassium.

Hydroxycitric acid:

MW: 208.12 g/mol

MF: C₆H₈O₈



(-)-Hydroxycitric acid

Therapeutic Uses:

The active constituent in this herb is called Hydroxycitric acid or HCA and is gaining a reputation for assisting weight loss through appetite suppression and by reducing the body's ability to form adipose (fatty) tissue during times of overeating.

* *Garcinia* has also been historically used to treat gastric ulcers. A 2002 study indicates this herb works primarily through the action of one of these plant's constituents, garcinol. Garcinol is known to lower acidity in the stomach and protects the gastric mucosa.

* The rind of *garcinia cambogia* is also astringent, which is why it was also historically used in the treatment of diarrhoea and dysentery as well as having the added benefit in the treatment of gastric and duodenal ulcers.

* The ability for *Garcinia's* component, HCA, to reduce

blood lipid levels and lower blood cholesterol is another feature of this amazing natural medicine. * More recently, it has been proposed that *Garcinia cambogia* has a hepato protective ability against external toxins, such as alcohol. A recent study showed that *Garcinia* prevented liver cells from becoming fibrotic and stopped cell damage caused by high blood lipid levels.

**Garcinia cambogia*, an exotic fruit grown in South India, has been used to impart a distinctive sour flavour to Indian cooking. It is the source for a revolutionary natural diet ingredient which is currently a rage in America, Japan, Europe and other western countries.

GARCINIA- THE ANTI-OBESITY DRUG: ^[6-9]

The *Garcinia* fruit is a rich source of hydroxycitric acid (HCA), the active agent that aids in weight loss by inhibiting fat production and suppressing appetite. *Garcinia* contains citrine, an extract that is 50-60% HCA, which inhibits an enzyme that helps the body synthesize fat for storage in adipose tissue. HCA promotes energy, inhibits lipogenesis, lowers the production of cholesterol and fatty acids, increases the production of glycogen in the liver, suppresses appetite, and increases the body's production of heat by activating the process of thermogenesis.

Garcinia cambogia extract is quickly becoming a popular ingredient in many weight loss supplements. Many studies have been pointing to strong possibilities that it will help some people to lose weight. But like similar studies, the evidence is not conclusive. In spite of this it is been cited in many weight loss supplements as been an active ingredient for losing weight. *Garcinia cambogia* belongs to the citrus family like oranges and lemons. It is a small tropical fruit that is too sour to eat but the rind is used as a spice in Indian cooking. It is indigenous to India and Africa. The active ingredient usually accredited for weight loss in this fruit is its extract, hydroxycitric acid. Hydroxycitric acid (HCA) unlike caffeine is not a stimulant. Neither is it an appetite suppressant, both of which work directly on the nerve centers of the brain. Both stimulants and appetite suppressants can have undesired side effects, including causing food binges any

time you stop taking them. Instead, HCA satisfies the body's need for energy and improves the signaling system that the body uses to tell the brain when it has eaten enough. In overweight people this response is often delayed, causing them to continue to eat more than they need. HCA seems to work best for people who overeat when they are anxious or stressed, as it will give the same calming effect that they get from food. Generally you do not need to eat any special foods when you are taking HCA, and there are no 'forbidden foods'. Choose healthy foods and you should find that you lose weight and fat slowly but steadily without really trying. You can take slightly smaller portions if you wish and choose fruit instead of sugary snacks but you should not need to go hungry. This is a very natural way to lose weight. *Garcinia cambogia* extract (HCA) in weight loss supplements is usually combined with chromium. Chromium is a mineral that is often lacking in our diets as we get older and a chromium deficit can contribute to weight gain and possibly diabetes. HCA and chromium seem to work in a positive synergy to regulate the body's blood sugar levels. However if you have diabetes already, you should see your doctor before taking any products containing chromium. Though HCA shows possibilities it is best to be cautious just like with all other weight loss supplements. For example do not take HCA if you are pregnant or breast feeding. Consult a doctor before giving it to children. You may also want to avoid HCA if you suffer from migraine or arthritis which can be worsened by citrus fruits.

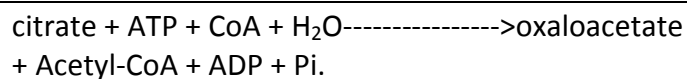
HCA has some significant advantages over many other weight loss supplements ingredients because it has been extensively tested in research laboratories on both human and animal subjects and no side effects have been found. Consequently it is considered a natural weight loss supplement.

PHARMACOLOGICAL ACTION OF GARCINIA CAMBOGIA. ^[10,11]

Normally the body converts carbohydrates (glucose, fructose, galactose) taken by meal into energy (ATP) and the excess carbohydrates that cannot

be used immediately for energy convert into glycogen. Glycogen is the storage form of carbohydrates, deposited in muscles and the liver.

When the glycogen stores are reasonably full, additional carbohydrates are then converted into excess of extramitochondrial Acetyl CoA required for fatty acid synthesis using ATP Citrate lyase enzyme.



(-)-Hydroxycitric acid [(-)-HCA] is the principal acid of fruit rinds of *Garcinia cambogia*

(-)-HCA was shown to be a potent inhibitor of ATP citrate lyase. The inhibition of this reaction limits the availability of acetyl-CoA units required for fatty acid synthesis and lipogenesis during a lipogenic diet, that is, a diet high in carbohydrates.

This added glycogen load in the liver stimulates a longer lasting neuro-signal from the liver to the brain, indicating satiety (satisfaction), thus helping to suppress appetite longer.

(-)-HCA as weight-controlling agent.

Inhibition of citrate lyase may aid aerobic endurance.^[12]

Owing to a substantial increase in glucose uptake by working muscle, glucose homeostasis during sustained aerobic exercise requires a several fold increase in hepatic glucose output.

As exercise continues and liver glycogen declines, an increasing proportion of this elevated glucose output must be provided by gluconeogenesis. Increased gluconeogenic efficiency in trained individuals is a key adaptation promoting increased endurance, since failure

of hepatic glucose output to keep pace with muscle uptake rapidly leads to hypoglycaemia and exhaustion.

Pre-administration of (-)-hydroxycitrate, a potent inhibitor of citrate lyase found in fruits of the genus *Garcinia*, may aid endurance during post-absorptive aerobic exercise by promoting gluconeogenesis.

Carnitine and bioactive chromium may potentiate this benefit. The utility of this technique may be greatest in exercise regimens designed to promote weight loss.

Potential Side Effects of *Garcinia Cambogia*:^[13]

Garcinia cambogia reportedly does not have any known adverse effects in healthy adults, but there are some people who are advised not to take it. According to experts, this includes children, pregnant and lactating women, those diagnosed

with diabetes mellitus, and people with Alzheimer's or other forms of dementia disease. In the case of Alzheimer's patients, it is thought HCA might form acetylcholine in the brain, while diabetics could be affected by HCA's tendency to lower blood sugar. Conversely, in healthy adults this latter effect can purportedly curb cravings for sweets and carbohydrates. And it is important to discuss this with your health care professional.

Therapeutic Dosages:

Supplements are available in various forms including tablets, capsules, powders, extracts and even snack bars. *Garcinia cambogia* medications are usually standardised to contain fixed percentage of HCA. The usual dosage for *garcinia* is 300 to 500mg tablets three times daily taken half an hour before meals with water.

SPECIFICATION OF GARCINIA CAMBOGIA

Botanical Name :	GARCINIA CAMBOGIA
Local Name :	Vilati Amlı
Plant part :	Fruit
Active Constituent :	Calcium salt of Hydroxy Citric Acid
Description	
Appearance :	pale brown powder
Aroma :	odourless
Taste :	Chalky herbal
Solubility :	Slightly soluble in hot water,

	Soluble in diluted acids, Insoluble in alcohol
Identification :	HCA Content NLT 50% By IR Spectrum Calcium by Titration NLT 18%
Type of Preparation :	Dry Herbal Extract
Specification	
Moisture :	NMT 5%
PH(1% w/v suspension) :	Between 7 & 10
Mesh size :	80
Loss on drying at 105° C :	NLT 3 %
Acid insoluble substances :	NMT 3%
Bulk density :	Between 0.50 & 0.70 gm/ml
Loose Bulk Density :	Between 0.30 & 0.50 gm/ml
Heavy Metals Arsenic :	< 1ppm
Mercury :	< 2ppm
Lead :	< 5ppm
Microbiological Analysis	
Total Bacterial count :	<1000 cfu/gm
Total fungal count :	< 500 cfu/gm
E. Coli, Staphylococcus Aureus :	Absent
Salmonella, Pseudomonas :	Absent
Pathogens, Aeruginosa :	Absent

CHARACTERIZATION OF (-) HYDROXY CITRIC ACID FROM

GARCINIA CAMBOGIA FRUIT EXTRACT.^[16]

Isolation of active constituent

Finely powdered aqueous extract of dried fruits of *Garcinia cambogia* was dissolved in double distilled water.

Pectins are removed by alcohol precipitation method and the filtrate was treated with 5 % potassium hydroxide solution and refluxed for three hours.

Potassium salt of HCA was precipitated out and collected by subsequent filtration and evaporation to get salt of potassium hydroxy citrate.

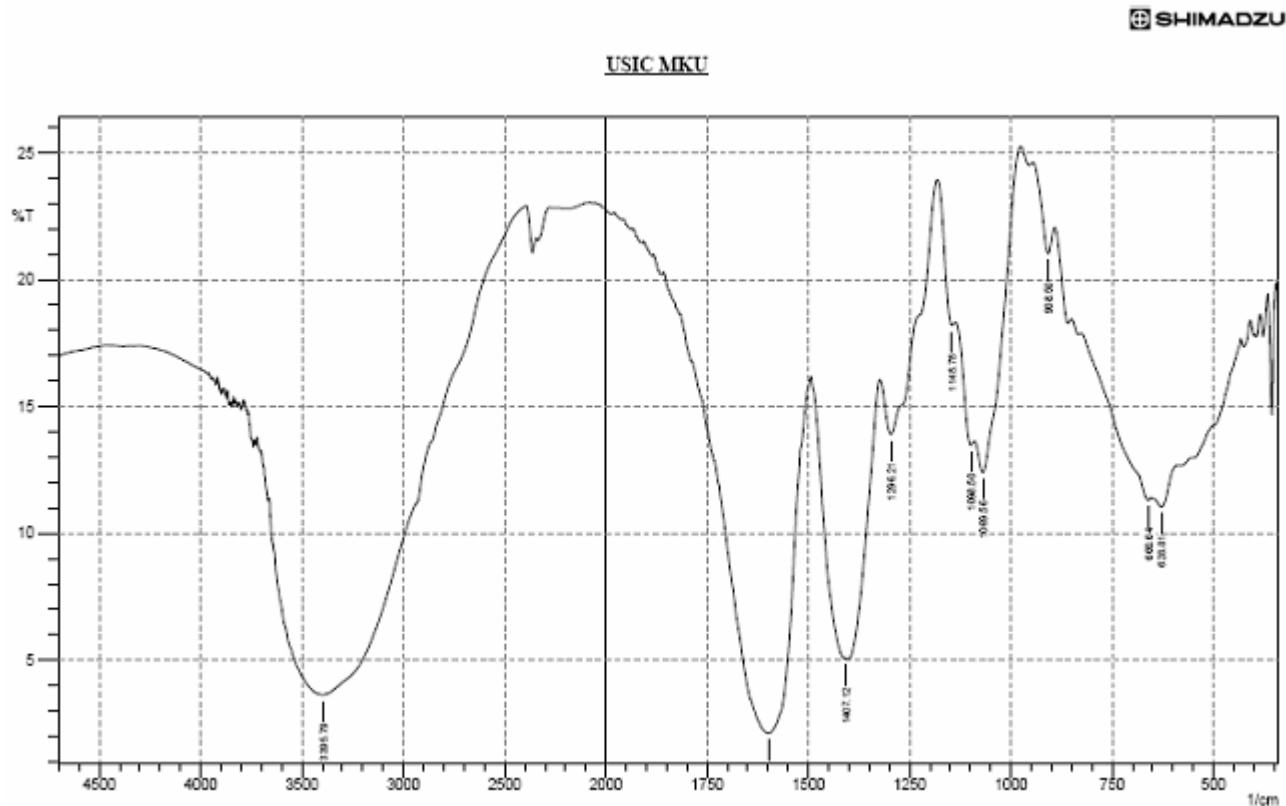
By UV-Visible Spectroscopy

The solution of 2 mg/ml concentration of HCA in 0.01N sulfuric acid was scanned between 200 –400 nm after passing through cation exchange resin (Amberlite IR120 H⁺ form) to liberate free acid.

By IR Spectroscopy

The potassium bromide dispersion of isolated potassium hydroxy citrate (Potassium salt of HCA) was prepared and the complete spectrum was scanned against blank disk.

The absorption and vibration bands were observed at various frequencies and reported graph (Fig.1) was compared with standard graph.

Fig.1. Infra Red Spectrum for isolated (-) Hydroxy citric acid from Garcinia cambogia fruit extract

The detection of spot was done by spraying with 1 % Sodium meta vanadate solution.

By Paper and Thin Layer Chromatography

Same concentration of isolated HCA and pure HCA solutions were applied as a spot on Whatman filter paper No.1 and Pre-coated silica gel plate.

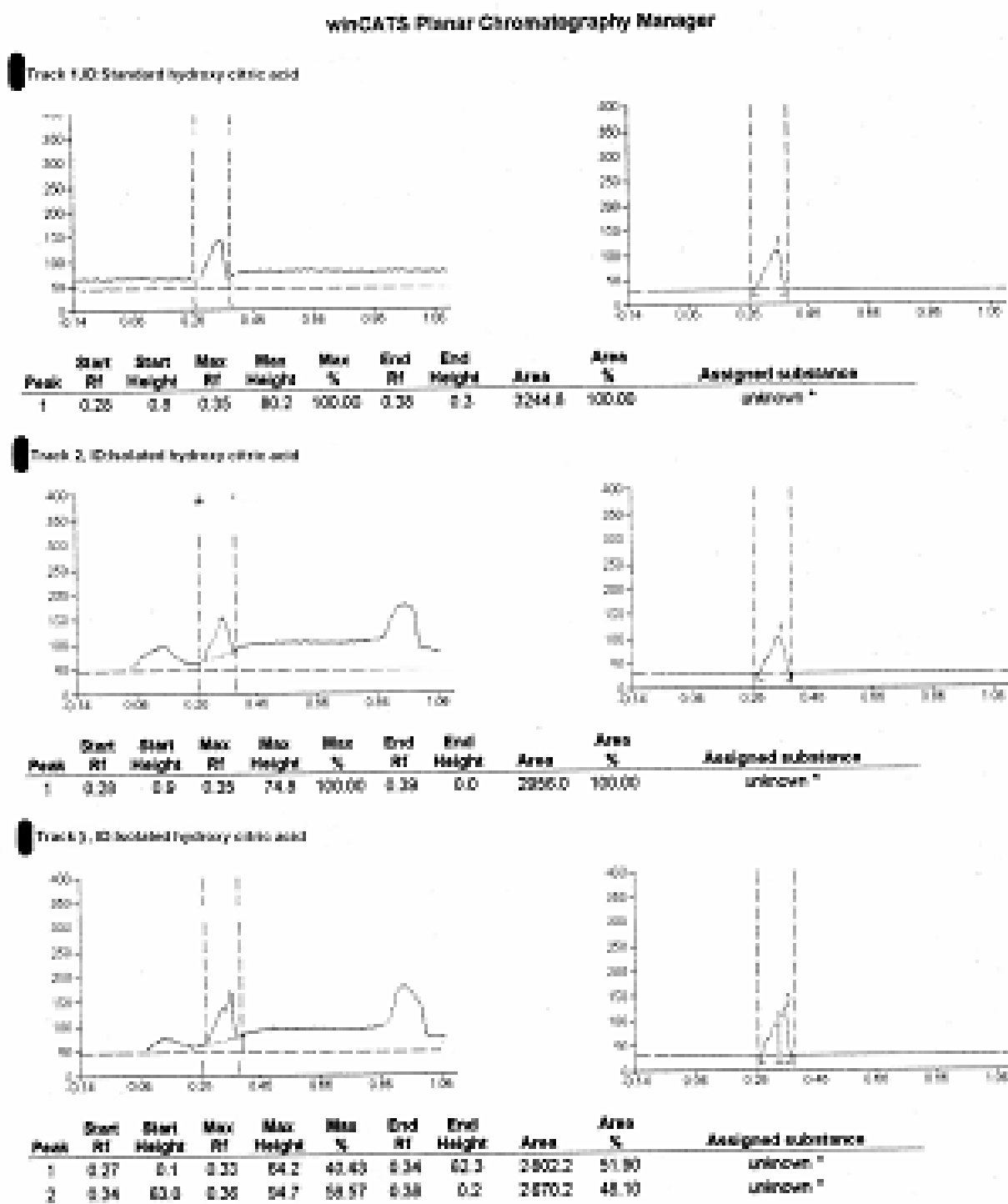
The chromatogram was developed using the solvent system of n-butanol:Acetic acid:water (4:1:5) for paper chromatography and n-butanol:Formic acid:water (4:2:4) for TLC.

By High Performance Thin Layer Chromatography

The chromatogram was developed with pre-coated silica gel plates using n-butanol:Formic acid:water (4:2:4) as mobile phase and scanned under 254 nm with 20 mm/s scanning speed.

The observed R_f values and areas of the peak were displayed on graph (Fig.2).

Fig.2. HPTLC graph for standard (-) Hydroxy citric acid and Isolated (-) Hydroxy citric



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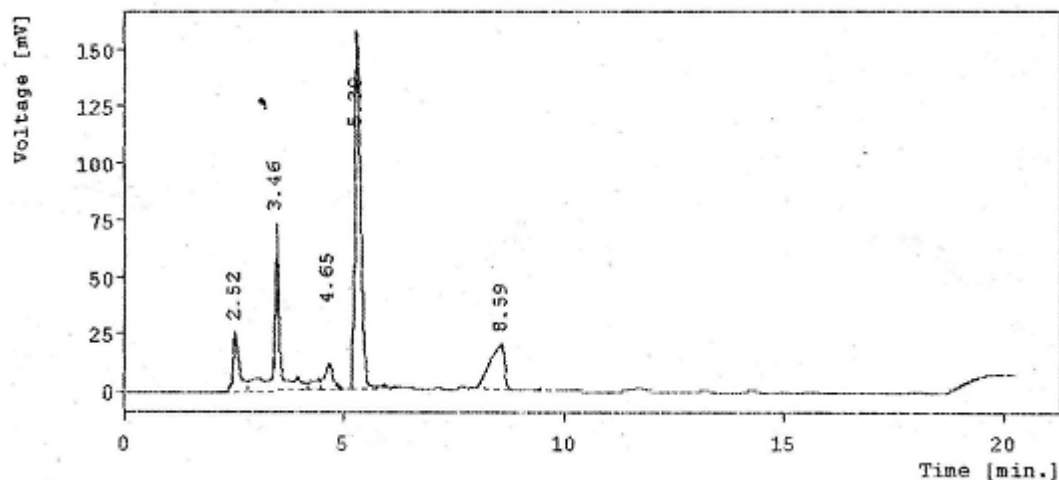
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Content analysis by High Performance Liquid Chromatography

2 mg/ml concentration of solutions were prepared from standard HCA and Garcinia cambogia fruit extract in 0.01N sulfuric acid and passed through cation exchange resin to get free acid.

20 µl solutions of standard and test were injected in RP-HPLC instrument using C18 column as stationary phase

Fig.3. HPLC graph for isolated (-) Hydroxy citric acid



RESULTS AND DISCUSSION:

Chemical nature and chemical structure of isolated HCA was observed by UV spectrum (λ max obtained at 204 nm) and IR spectrum (Fig.1) and was confirmed with respective standard drug.

HCA was identified by observing the orange spot at Rf value of 0.26 for paper chromatography and 0.35 for TLC.

The Rf values obtained in the TLC was again confirmed by HPTLC analysis (Fig.2) using same solvent system as per Thin layer chromatography.

The absorbance maximum was observed at 204 nm; hence 204 nm was used for HPLC detection.

Some other minor peaks were also observed which may be due to other acids present in plant. HCA was resolved as single peak (Fig.3) and confirmed by spiking with standard HCA.

Content of HCA in fruit extract was found to be 42 – 44 %. The above method was validated by intra-day and inter-day precision studies and %RSD was found to be 0.9206 and 1.1073 respectively.

and 0.01N sulfuric acid as mobile phase at a flow rate of 1.0 ml/min with UV detection at 210 nm.

The resultant graph was shown at Fig.3. The percentage content of HCA in fruit extract was calculated and the proposed method was validated by carrying the intra-day and inter-day precision studies.

COMPARISON BETWEEN HERBAL AND SYNTHETIC DRUGS:

Synthetic Drugs:

Sibutramine:^[17,18]

Sibutramine (usually in the form of the hydrochloride monohydrate salt) is an oral anorexiant.

Sibutramine is a neurotransmitter reuptake inhibitor that reduces the reuptake of serotonin (by 53%), norepinephrine (by 54%), and dopamine (by 16%), serotonergic action, in particular, is thought to influence appetite thereby increasing the levels of these substances in synaptic clefts and helping enhance satiety; the

Side effects

A higher number of cardiovascular events have been observed in people taking sibutramine versus control (11.4% vs. 10.0%).

In 2010 the FDA noted the concerns that sibutramine increases the risk of heart attacks and strokes in patients with a history of cardiovascular disease.

Frequently encountered side effects are: dry mouth, paradoxically increased appetite, nausea, strange taste in the mouth, upset stomach, constipation, trouble sleeping, dizziness, drowsiness, menstrual cramps/pain, headache, flushing, or joint/muscle pain.

Sibutramine can substantially increase blood pressure and pulse in some patients. Therefore regular monitoring needs to be performed.

The following side effects are infrequent but serious and require immediate medical attention: cardiac arrhythmias, paresthesia, mental/mood changes (e.g., excitement, restlessness, confusion, depression, rare thoughts of suicide).

Symptoms that require urgent medical attention are seizures, problems urinating, abnormal bruising or bleeding, melena, hematemesis, jaundice, fever and rigors, chest pain, hemiplegia, abnormal vision, dyspnea and edema.

Orlistat ^[19,20]

Orlistat is used for the treatment of obesity. The amount of weight loss achieved with orlistat varies. In one-year clinical trials, between 35.5% and 54.8% of subjects achieved a 5% or greater decrease in body mass, although not all of this mass was necessarily fat.

Its primary function is preventing the absorption of fats from the human diet, thereby reducing caloric intake.

Mechanism of Action:

Orlistat works by inhibiting gastric and pancreatic lipases, the enzymes that break down triglycerides in the intestine. When lipase activity is blocked, triglycerides from the diet are not hydrolyzed into absorbable free fatty acids, and are excreted undigested instead.

Side Effects:

The primary side effects of the drug are gastrointestinal-related, and include steatorrhea (oily, loose stools with excessive flatus due to unabsorbed fats reaching the large intestine), fecal incontinence and frequent or urgent bowel movements.

An analysis of over 900 orlistat users in Ontario showed that their rate of acute kidney injury was more than triple that of non-users.

The putative mechanism for this effect is postulated to be excessive oxalate absorption from the gut and its subsequent deposition in the kidney, with excessive oxalate absorption being a known consequence of fat malabsorption.

A 2006 animal study linked orlistat with aberrant crypt foci (ACF), lesions found in the colon which is believed to be one of the earliest precursors of colon cancer.

Phentermine: ^[21-23]

Phentermine, a contraction of "phenyl-tertiary-butylamine", is an appetite suppressant of the phenethylamine class.

It is an amphetamine like stimulant.

It is approved as an appetite suppressant to help reduce weight in obese patients when used short-term and combined with exercise, diet, and behavioral modification.

It is typically prescribed for individuals who are at increased medical risk because of their weight and works by helping to release certain chemicals in the brain that control appetite.

Mechanism of Action:

Phentermine works on the hypothalamus portion of the brain to stimulate the adrenal glands to release norepinephrine, a neurotransmitter or chemical messenger that signals a fight-or-flight response, reducing hunger.

Phentermine works outside the brain as well to release epinephrine or adrenaline causing fat cells to break down stored fat, but the principal basis of efficacy is hunger-reduction.

At clinically relevant doses, phentermine also releases serotonin and dopamine, but to a much lesser extent than that of norepinephrine.

Adverse Effects:

Generally, phentermine appears to be relatively well tolerated. It can produce side effects consistent with its catecholamine-releasing properties, e.g., tachycardia (increased heart rate) and elevated blood pressure, but the incidence and magnitude of these appear to be less than with the amphetamines.

Because phentermine acts through sympathomimetic pathways, the drug may increase blood pressure

and heart rate. It may also cause palpitations, restlessness, and insomnia.

Additionally, phentermine has the potential to cause psychological dependence. After short term use, tolerance begins and can be followed by rebound weight gain.

More common side effects:

Cardiovascular: Primary pulmonary hypertension and/or regurgitant cardiac valvular disease, palpitation, tachycardia, elevation of blood pressure.

Central Nervous System: Overstimulation, restlessness, dizziness, insomnia, euphoria, dysphoria, tremor, headache.

Gastrointestinal: Dryness of the mouth, unpleasant taste, diarrhea, constipation, other gastrointestinal disturbances.

Allergic: Urticaria, endocrine Impotence, changes in libido.

Herbal Drugs:

Herbal Drugs is a traditional medicinal or folk medicine practice based on the use of plants and plant extracts.

Garcinia cambogia:

Botanical Name: Garcinia cambogia

Family: Guttiferae

Description: Garcinia cambogia extract is the calcium salt of hydroxy citric acid (Both 50% and 60% hydroxy citric acids are available), which is obtained from water extract of Garcinia cambogia fruit .

It is non-toxic, tasteless, odorless powder and found to be very effective herbal medicine for controlling obesity and cholesterol by inhibiting lipogenesis in our body.

It is a well established fat burning agent all over the world.

Potential Side Effects of Garcinia Cambogia:

There are no known side effects for using this herb, however, it is not recommended for diabetics or people suffering any dementia syndrome, including Alzheimer's; and in pregnant and lactating women. Garcinia cambogia does have contraindications with certain medications, and it is important to discuss this with your health care professional.

Guggul: ^[24,25]

Botanical Name: Commiphora mukul

Family: Burseraceae.

Common Name(s): Guggul , guggal , gum guggal , gum guggulu , gugulipid

Description: Guggul is an herb that has been used in traditional Ayurvedic medicine for centuries in the treatment of obesity.

Guggul can help stimulate thyroid activity, which can increase metabolism causing weight gain. It is recommended to take 25 mg of guggul, three times a day, to promote weight loss.

Weight Loss Activity:

Guggul promotes weight loss, according to a study produced by the Department of Biomedical and Pharmaceutical Sciences in the College of Pharmacy of the University of Rhode Island, published in a 2007 edition of "Cardiovascular Drug Reviews."

This study found that guggul increases the reactions between bile acids and lipids, which are the dietary fats found in the foods you consume. These reactions speed up the elimination of lipids before they can be absorbed during digestion, which promotes weight loss.

Guggulsterone has been shown to stimulate thyroid activity. This effect has been used to promote gugulipid as a weight loss product that increases the body's rate of metabolism.

Uses:

Traditionally used to treat arthritis, obesity, and other disorders, guggul has been shown to lower cholesterol and triglycerides and to stimulate thyroid activity in a few small studies.

Adverse Reactions:

While the human safety profile (including children, pregnant or nursing women, and patients with severe hepatic or renal disease) of the extract has not been well described, no significant adverse events were reported in clinical studies; the adverse effects were primarily GI and several cases of headache, hiccup, and rash.

Cissus quadrangularis: ^[26]

Cissus quadrangularis is a perennial plant of the grape family. It is commonly known as Veldt Grape or Devil's Backbone.

There are several reports on Cissus quadrangularis use in the management of obesity.

Various formulations now contain extract of *Cissus quadrangularis* in combination with other compounds, used for the purpose and weight management.

Cissus quadrangularis stems and leaves contain specific flavanoids and indanes which inhibit lipase, amylase and alpha-glucosidase activity in a mammal, therefore contributing to weight loss.

Side Effects:

Gastrointestinal Problems: These include flatulence and diarrhea.

Dry mouth, Headache and insomnia

CONCLUSION:

Obesity is a major problem in the affluent societies of developing and developed world and the Health Risks associated with the obesity are

Type 2 diabetes, Heart disease, Stroke High blood pressure, High blood cholesterol, etc.

To get rid of these diseases it is necessary to avert obesity.

From the above discussion it is proposed that herbal drugs are more beneficial in treatment of obesity because of its fewer side effects and to prevent diseases like Type 2 diabetes, Heart disease, Stroke High blood pressure before their occurrence.

EXPERIMENTAL WORK:

The experimental work has been performed in the laboratory of Indore Institute Of Pharmacy, Indore (M.P.)

Solubility:

Water:	Slightly soluble
Ethanol:	Insoluble
Methanol:	Insoluble
Chloroform:	Precipitate
Sulfuric acid:	Freely Soluble
Hydrochloric Acid:	Freely Soluble
Carbon Tetrachloride:	Precipitate
Isopropyl Alcohol:	Insoluble
Diethyl Ether:	Precipitate.

Absorbance:

2 µg/ml in 0.1N HCl was found to be 206 nm and absorbance was found to be 0.46.

RESULTS:

The extract is soluble in HCl and Sulfuric Acid.

The lambda max. was found to be 206 nm in 0.1N HCl

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