Review Article

Hypolipidemic Potential of Herbal Drugs (Lagenaria siceraria & *Carica papaya*) and Cow Urine: A Review

Pankaj Kumar*[1], Shailendra Sharma[2]
[1]Adesh Institute of Pharmacy and Biomedical Sciences, Adesh University, Bathinda, Punjab, India.
[2]Jodhpur Institute of Pharmacy, Jodhpur National University, Jodhpur, Rajasthan, India.
***Corresponding author's E-mail:** pankaj1981sameer@gmail.com

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ABSTRACT

Hyperlipidemia plays an important role in the development of atherosclerosis, the main cause of death in the world. We study the lipid-lowering effect of *Carica papaya, Lagenaria siceraria* and cow urine. Plants have been used by mankind as remedies from the beginning of civilization. The uses of medicinal plants as traditional medicine are well known. This is mainly due to the presence of bioactive metabolite in plants which formed the basis of herbal medication the juice of fresh fruits of *Lagenaria siceraria* for antihyperlipidaemic activity by evaluating the blood cholesterol level of atherogenic diet rat and proved that juice of the fresh fruits of *Lagenaria siceraria* have the potent effect to cause a blood cholesterol lowering effect and the serum biochemistry changes may suggest that the juice extract t has a tonic effect on the kidneys and the liver and their organs play central role in drug metabolism. Administration of *Carica papaya* produced a significant improvement in the lipid profile by lowering total cholesterol, LDL and triglycerides and by increasing HDL level thus helping in retarding the secondary complications. It has anti-lipidemic and anti-cholestrolemic activities and as such could be used in the management of hypercholesterolemia. This study thus, supports the acclaimed use of the plant in the management of hypertension. The cow urine therapy is capable of curing several curable and incurable diseases. Cow's urine also called Gomutra is recommended as a healing aid in Ayurveda. A person falls ill when there is deficiency (alteration) of the substances inside the body. The cow urine contains those substances, which are present in the human body. Therefore, consumption of cow urine maintains the balance of these substances and cures incurable diseases. In the present study we have found that cow urine consumption significantly reduced the elevated lipid profiles in human and animals.

Keywords: Hypolipidemic potential, phytoconstituents, herbal drugs, *Lagenaria siceraria*, *Carica papaya,* cow urine.

INTRODUCTION

Hyperlipidemia refers to elevated levels of lipids and cholesterol in the blood, and is also identified as dyslipidemia to describe the manifestations of different disorders of lipoprotein metabolism.[1] Hyperlipidemia is a condition of excess fatty substances called lipids, largely cholesterol and triglycerides in the blood. It is also called hyperlipoproteinemia because these excess lipids travel in the blood attached to proteins. These fatty substances can remain dissolved while in circulation.[2] It is a disorder of lipid metabolism manifestated by elevation of plasma concentrations of the various lipid and lipoprotein fraction, which is the key risks factors for cardio vascular disease (CVD). It is also defined as an elevation of one or more of the following cholesterol esters, Phospholipids or triglycerides. Abnormalities of plasma lipids can result in predisposition to Coronary, cerebrovascular and peripheral vascular arterial diseases and has been reported & has most common cause of death in developed as well as developing nations.[3] Hyperlipidemia may be classified as either familial (also called primary) caused by specific genetic abnormalities, or acquired (also called secondary)when resulting from another underlying disorder that leads to alterations in plasma lipid and lipoprotein metabolism. Also hyperlipidemia may be idiopathic that is without known cause. Medicinal plants have always been considered as healthy source of life for all people due to its rich therapeutic properties and being 100% natural. Medicinal plants are widely used by majority of populations to cure various diseases and illness and have high impact on the world's economy.[2] The plant extracts and their constituents plays the major role in traditional medicines and therapies.[3] Number of studies are there reporting the hypolipidemic activity of various traditional medicines from different regions of India. The present review constitutes of plants with hypolipidemic activity *Lagenaria siceraria* fruit is used as a vegetable in India. The fruit is traditionally used as a cardio tonic, aphrodisiac and general tonic and liver tonic and against liver disorders and pain, anti-inflammatory, expectorant and diuretic agent. Further, antihepatotoxic activity of fruit pulp, analgesic and anti-inflammatory activity of fruit juice and hypolipidimic activity of the fruit have also been evaluated. Recently, the antioxidant activity of ethanolic extract of epicarp and fresh juice of *L. siceraria* fruit has been reported.

Lagenaria siceraria

Lagenaria siceraria (Molina) Standley syn. *L. leucantha Rusby*; *L. Vulgaris Ser*. (Family: Cucurbitaceae) are commonly known as Bottle gourd, an excellent fruit in the nature having composition of all the essential constituents that are required for normal and good health of humans. It cures pain, ulcers, fever, asthma, and other bronchial disorders. It also cures pain, ulcers, fever, and

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used for pectoral cough, asthma and other bronchial disorders. *L. siceraria* fruit is traditionally used for its cardio protective, cardio tonic, general tonic, aphrodisiac and acts as alternate purgative, diuretic, cardiovascular disorder is claimed to be relieved following regular intake of bottle gourd juice for about 4-6 months. The fruits are edible and considered as good source of vitamin C, â-carotene, vitamin B-complex, pectin and also contain highest choline level- a lipotropic factor. Modern phytochemical screening methods showed the presence of triterpenoid cucurbitacins B, D, G, H and reported to contain saponins, essential fixed oils, vitamins. Decoction of leaves, mixed with sugar given in jaundice. Seeds are nutritive and diuretic, are used in dropsy and as anthelmentic, roots also in the treatment of dropsy. The seeds (wt of 100 seeds, 15 gm) are edible. In china, they are boiled in salt water and eaten as an appetizer. The seed oil is applied in headache. A decoction of *L. siceraria* is employed in the treatment of anasarca, ascites and beriberi.[8]

Lagenin- a novel ribosome inactivating protein has been isolated from the lyophilized water extract of seeds which is known to possess immunosuppressive, antitumour, antiviral, antiproliferative and anti-HIV activities.

Taxonomical classification [9]

- **Kingdom**: Plantae
- **Division:** Magnoliophyta
- **Class:** Magnoliopsida
- **Order**: Cucurbitales
- **Family**: Cucurbitaceae
- **Genus**: *Lagenaria*
- **Species**: *L. siceraria*
- **Part used**: Fruit

Figure: 1 *Lagenaria siceraria* plant with fruits

Botanical description

Lagenaria is a pubescent, climbing or tailing herb with stout 5- angled stems and bifid tendrils, found throughout India, either wild or cultivated. Leaves are long, petioled, 3-5 lobed, 10-12 cm and hirsute. Fruits are large, up to 1.8m. Long, fruit bottle shaped with a hard shell- like epicarp when ripe, numerous seeds, long, white, smooth, 1.6- 2.0 cm long, horizontally compressed with marginal groove. Flowers are white, solitary, axillary unisexual. Male flowers posses botanical description of calyx and campanulate, tube narrow, lobes 5, linear, petals 5, free, white, stamens 3. Female flowers possess botanical description of calyx and carola as in male flowers. Overy densely villous, style thick, stigmas and bilobed.

Microscopy

Transverse section of *Lagenaria siceraria* leaf showed following features- upper epidermis consists of elongated parenchymatous cells covered by cuticle. Lower epidermis- contains elongated wavy walled parenchymatous cells covered by cuticle. Number of Covering and collapsed trichomes are present while very few glandular trichomes are also present. Upper epidermis shows few stomata which are of anisocytic type. Palisade cells are present at upper and lower epidermis. It shows hexagonal to polygonal, large and thin walled colourless cells and may be water storing. Mesophyll is made up of 3-4 layered chloroplasts containing, compactly arranged, oval to circular cells. It is interrupted by vascular bundles of various sizes. Vascular bundles - Vascular bundles are surrounded by 2-3 layered sclerenchyma. They are conjoint, collateral and closed. Xylem is placed towards upper epidermis and phloem towards lower epidermis.[11]

Habitat

The cultivated form of *L. siceraria* is considered to be of African and Asian origin. *L.siceraria* popular vegetable, grown almost all the year round, particularly in frost free areas. It can be cultivate in all kinds of soil but thrives best in heavily manured loams. It required warm humid climate or plenty of watering when grown during dry weather. Seeds may be sown in nursery beds and seedlings transplanted when they have put forth 2-3 leaves. They may be also sown directly 4-5 seeds together in mannured beds or pits 5-6ft. apart the strongest among the seedlings is retained while others are removed and transplanted. Seedling transplantation is where an early crop is desired, generally two crop raised in India; the summer crop is sown from the middle of October to the middle of March and the later crop, from the beginning of March to the Middle of July. Round fruit types are usually sown for the early crop and bottle–shaped types for the second crop. Vines are allowed to trail on the ground or trained over walls. Trees or other support trailing over give high yield of fruit.

Synonyms

- **Sansk**: Alabu, Tumbi Ishavaaku, Katutumbi, Tiktaalaabu, alaabu.
- **Beng**: Laus, Lokitumbi,
- **Eng**: Bottle Gourd
- **Guj** : Dudi, Tumbadi
- **Hindi**: Lauki, Ghia
- **Kan**: Isugumbala, Tumbi
- **Mal**: Chorakka, Churan, Choraikka, Piccura, Tumburini, Cura, Tumburu
- **Mar**: Phopla
- **Punj**: Tumbi, Dani
- **Tam**: Shorakkai, Surai, Suraikkai

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- **Tel**: Sorakaya, Anapakaya
- **Urdu**: Ghiya, Lauki

Ayurvedic description

- **Rasa**: Madhura;
- **Guna**: Snigdha;
- **Virya**: Sita;
- **Vipaka**: Madhura;
- **Karma**: Pittahara, Kaphahara, Bhedaka, Rucikara, Hradya,Vrsya.
- **Therapeutic uses**: Jwara, Kasa, Svasa, Visa roga, Sopha, Vrana, Sula.

Phytoconstituents of *Lagenaria siceraria*

The phytochemical analysis of edible portion of the fruit it is shown that it is a good source Glucose and fructose. The amino acid composition of the fruit is as follows: leucines 0.8; phenylalanine 0.9; valine 0.3; tyrosine 0.4; alanine 0.5; threonine 0.2; glutamic acid 0.3; serine 0.6; aspartic acid 1.9; cystine 0.6; cysteine 0.3. The fruit is a good source of vitamins B and a fair source of ascorbic acid. Bitter fruits yield 0.013% of solid foam containing cucurbitacins B, D, G and H, mainly cucurbitacin B. These bitter principles are present in the fruit as aglycones. Leaves contain cucurbitacin B and roots, cucurbitacins B, D and E. *Lagenaria siceraria* shows presence of flavone-C glycoside. A water soluble polysaccharide, isolated from fruiting bodies of *Lagenaria siceraria*, is composed of methyl-α-d-galacturonate, 3-O-acetyl methyl-α-dgalacturonate, and β-d-galactose in a ratio of nearly 1:1:1. This polysaccharide showed cytotoxic activity in-vitro against human breast adenocarcinoma cell line.

Antihyperlipidemic activity

Antihyperlipidemic activity of the fruit extracts in triton-induced hyperlipidemic rats and hypolipidemic effect in normocholesteremic rats were investigated. In the study, four different extracts viz. petroleum ether, chloroform, alcoholic, and aqueous extracts were prepared. Oral administration of the extracts dose dependently inhibited the total cholesterol, triglycerides, low-density lipoproteins level, and significantly increased the high-density lipoproteins level. Both the chloroform and alcoholic extracts exhibited significant effects compared others. However, the petroleum ether extract did not show significant effects. Antihyperlipidemic activity Nainwal et al.,(2011), evaluated the juice of fresh fruits of *Lagenaria siceraria* for antihyperlipidaemic activity by evaluating the blood cholesterol level of atherogenic diet rat and proved that juice of the fresh fruits of *Lagenaria siceraria* have the potent effect to cause a blood cholesterol lowering effect and the serum biochemistry changes may suggest that the juice extract has a tonic effect on the kidneys and the liver and theirorgans play central role in drug metabolism.[14] Ghuleet al.,(2009), evaluated antihyperlipidemic effect of the methanolic extract from *Lagenaria siceraria* fruit in hyperlipidemic rats and proved that at the 30th day most significant reduction in lipid levels in the LSFE treated rats as compared to the rats fed with high-fat diet at the 0thday and shows that the increase in weight in rats administered with LSFE was less when compared to rats fed with high-fat diet.[15,16] Deshpande JR et al. (2008) has been reported antihyperglycemic activity of *Lagenaria siceraria* (EELS) fruit. Hyperglycemia was induced in rats by alloxan monohydrate (150mg/kg, ip single dose). Rats in which hyperglycemia (blood glucose level above 260 mg/dl) was induced after 48 hr of alloxan administration were divided into 5 groups of 6 rats each. Group l served as the normal control and Group 2 as a hyperglycemic control to which saline solution was administered. Animals in Group 3 and 4 were hyperglycemic and treated with EELS (100 and 200 mg/kg po) for 14 days. Group 5 was treated with glibenclamide (5mg/ kg po) for 14 days. Plasma level of glucose were analysed on 0,7and 14th day of treatment, the percentage reduction by glibenclamide was 57.8 and 64.3% on 7th and 14th days respectively. Alloxan elevated serum lipid levels of total cholesterol (TC), trigycerides (TGL), low density lipoprotein \ (LDL-C) and very low density lipoprotein cholesterol (VLDL-C) and reduced that of high density lipoprotein cholesterol (HDL-C). Administration of ethanolic extract of *Lagenaria siceraria* (EELS) (100 and 200 mg/kg) effectively prevent these changes.[16]

Preparation of Hydroalcholic Extract (*Lageneria siceraria*)

The fresh fruit of LS was sliced, shade dried and coarsely powdered. A known amount (20g) of the coarse powder was packed in a clean dry soxhlet apparatus. The packed material was extracted with water and ethanol in a 1:1 ratio to obtain hydroalcoholic extract. The completion of extraction was determined by the absence of colours in the side arm of soxhlet apparatus by testing the siphoned solution for absence of any residue on evaporation to dryness. The extract obtained was collected in dry and previously weighed china disk. The solvent was evaporated to dryness on a water bath. After drying the china disk was re-weighed. This procedure was repeated five times to obtained sufficient amount of the extract and yield was calculated as given below-

Weight of china disk= 57.550 gm

Weight of china disk with extract =66.228 gm

Weight of coarse powder to be taken for extraction=20 gm

$$\% \text{ Yield} = \frac{\text{Weight of china disk with extract-Weight of China disk x 100}}{\text{Weight of coarse powder to be taken for extraction}}$$

$$\% \text{ Yield} = (66.228-57.550)*100/20$$

$$= 43.39 \% \text{ w/w}$$

Preparation of Fruit Juice

The fresh fruit juice of the *L. siceraria* was obtained by crushing the fresh fruits in the mixer. The crushed fruit

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was then filtered through muslin cloth and further used for study. This procedure was repeated throughout the entire treatment period.

The extract was dissolved in water and fresh juice was prepared and further used for following qualitative chemical evaluations.

Evaluation of Chemical Constituents of Extract and Juice of *Legeneria Scicereria*

Tests of carbohydrates

Table: 1 Tests for carbohydrates

S. No.	Identification test	Observation	Inference
1.	**Molisch test-** **Extract-**2-3 ml of aqueous solution of extract +few drops of alcoholic solution of α-naphthol and add conc. H_2SO_4	Violet ring was formed at the junction of two liquids.	Carbohydrate was present.
	Juice-2-3 ml of juice +few drops of alcoholic solution of α-naphthol and add conc. H_2SO_4	Violet ring was formed at the junction of two liquids.	Carbohydrate was present
2.	**Test for reducing sugar** **Benedict's Test-** **Extract**-Equal volume of Benedict's reagent and aqueous solution of extract were mixed. Heated on boiling water bath for 5 min.	Solution appeared greenish.	Reducing sugar was present
	Juice- Equal volume of Benedict's reagent and juice were mixed. Heated on boiling water bath for 5 min	Solution appeared greenish.	Reducing sugar was present

Test for Terpenoids

Table: 2 Test for Terpenoids

S. No.	Identification test	Observation	Inference
1.	**Salkowaski test-** **Extract-**Aqueous solution of extract was evaporated to dryness. To the residue 2 ml of chloroform and 2ml of conc.H_2SO_4 was added. Chloroform layer was shaked well.	Chloroform layer was appeared red and acid layer was showed greenish yellow fluorescence.	Terpenoids was present.
	Juice-Juice was evaporated to dryness. To the residue 2 ml of chloroform and 2ml of conc.H_2SO_4 was added. Chloroform layer was shaked well.	Chloroform layer was appeared red and acid layer was showed greenish yellow fluorescence.	Terpenoids was present.

Test for Protein

Table: 4 Test for Protein

S. No.	Identification test	Observation	Inference
1.	**Biuret test-** **Extract-**In 3 ml of aq sol. of extract add 4% NaOH & few drops of 1% $CuSO_4$.	violet color was not appeared	Protein was absent
	Juice-In 3 ml juice add 4% NaOH & few drops of 1% $CuSO_4$	violet color was appeared	Protein was present

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Test for C- Glycosides

Table: 3 Test for C- Glycosides

S. No.	Identification test	Observation	Inference
1.	**Modified Borntrager's test for C- Glycoside-** **Exract-**In aqueous extract 5 ml of 5% of $FeCl_3$ and dil. HCl was added. Heated for 5 min. in water bath cooled. Benzene was added, and shaked well. Organic layer was separated, dil. Ammonia was added.	Ammonical layer showed pinkish red color.	C- Glycoside was present.
2.	**Juice-**In juice 5 ml of 5% of $FeCl_3$ & dil. HCl was added. Heated for 5 min. in water bath cooled. Benzene was added and shaked well. Organic layer was separated, dil. Ammonia was added	Ammonical layer showed pinkish red color.	C- Glycoside was present.

Test for Alkaloids

Table: 6 Test for Alkaloids

S. No.	Identification test	Observation	Inference
1	**Mayer's test:** Extract/Juice+Pot. Mercuric Iodine Solution	No cream ppt	Alkaloid was absent
2	**Wagner's test:** Extract/Juice+iodine pot.iodide	No reddish brown ppt	Alkaloid was absent
3	**Dragendrorff's test:** Extract/Juice+Pot. Bismuth iodide solution	No brown ppt	Alkaloid was absent
4	**Hager's test:** Extract/Juice+Picric acid solution	No yellow ppt	Alkaloid was absent

Carica papaya

Papaya is a powerhouse of nutrients and is available throughout the year. It is a rich source of three powerful antioxidant vitamin C, vitamin A and vitamin E; the minerals, magnesium and potassium; the B vitamin pantothenic acid and folate and fiber. In addition to all this, it contains a digestive enzyme papain the effectively treats causes of trauma, allergies and sports injuries. All the nutrients of papaya as a whole improve cardiovascular system, protect against heart diseases, heart attacks, strokes and prevent colon cancer. The fruit is an excellent source of beta carotene that prevents damage caused by free radicals that may cause some forms of cancer.

Botanical description

The papaya, papaw, or pawpaw is the fruit of the plant *Carica papaya*, the only species in the genus Carica of the plant family Caricaceae.

Taxonomical Classification

- **Domain** Flowering plant
- **Kingdom** Plantae
- **Subkingdom** Tracheobionta
- **Class** Magnoliopsida
- **Subclass** Dilleniidae
- **Division** Magnoliophyta
- **Subdivision** Spermatophyta
- **Phylum** Steptophyta
- **Order** Brassicales
- **Family** Caricaceae
- **Genus** Carica
- **Botanical name** *Carica papaya* Linn.

It is native to the tropics of the Americas. The papaya is a large, tree-like plant, with a single stem growing from 5 to 10 m (16 to 33 ft) tall, with spirally arranged leaves confined to the top of the trunk. The leaves are large, 50–70 cm in diameter, deeply palmately lobed, with seven lobes. The tree is usually unbranched, unless lopped. The flowers appear on the axils of the leaves, maturing into large fruit. The fruit is ripe when it feels soft and its skin has attained amber to orange hue. Fresh green leave is an antiseptic, whilst the brown dried pawpaw leaf is the best as a tonic and a blood purifier. Chewing the seeds of ripe pawpaw fruit is used to lcean nasal congation, the green and dried pawpaw has a therapeutic value due to its antiseptic quality it cleans the intestine from bacteria. More so that the tea prepared with the green papaya leaf promotes digestion and it's the in the treatment of ailments such as chronic and indigestion, overweight and obesity, arthriochlorisis and high blood pressure and weakening of heart.

Microscopy

Figure 2: Papaya Plant

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Papaya belongs to a group of plant species known as laticiferous plants. These plants contain specialized cells (laticifers), dispersed throughout most plant tissues, that secrete a substance known as 'latex'. Latex is a complex mixture of chemical compounds with diverse chemical activities. Collectively, these compounds are thought to be involved in defence of the plant against a wide range of pests and herbivores (El Moussaoui et al. 2001).

The latex of papaya plants is rich in enzymes known cysteine proteinases, which are used widely for protein digestion functions in the food and pharmaceutical industries. Commercially, papaya latex is harvested from fully grown but unripe fruit, the skin of which contains numerous laticifers. Ripe papaya fruit contains no latex (Villegas 1997), possibly because the latex-producing cells cease functioning or breakdown with age. Cysteine proteinases may constitute as much as 80% of the enzyme fraction in papaya latex (El Moussaoui et al. 2001). The most well studied proteinases from papaya are papain, chymopapain, caricain and glycyl endopeptidase. Other enzymes known from papaya latex include glycosyl hydrolases such as -1,3-glucanases, chitinases and lysozymes, protease inhibitors such as cystatin and glutaminyl cyclotransferases and lipases (El Moussaoui et al. 2001). Unripe papaya fruit, papaya seeds and latex extracts have been implicated in numerous toxic and allergenic responses in mammals, including humans.

Habitat

Papaya plants grow in three sexes: male, female, hermaphrodite. The male produces only pollen, never fruit. The female will produce small, inedible fruits unless pollinated. The hermaphrodite can self-pollinate since its flowers contain both male stamens and female ovaries. Almost all commercial papaya orchards contain only hermaphrodites.[24] Originally from southern Mexico (particularly Chiapas and Veracruz), Central America, and northern South America,[25] the papaya is now cultivated in most tropical countries. In cultivation, it grows rapidly, fruiting within three years. It is, however, highly frost-sensitive, limiting its production to tropical climates. Temperatures below −2 °C (29 °F) are greatly harmful if not fatal. In Florida and California, growth is generally limited to southern parts of the states. In California, it's generally limited to private gardens in Los Angeles, Orange, and San Diego Counties. It also prefers sandy, well-drained soil, as standing water will kill the plant within 24 hours.[26] For cultivation, however, only female plants are used, since they give off a single flower each time, and close to the base of the plant, while the male gives off multiple flowers in long stems, which result in poorer quality fruit.[27] Gaining in popularity among tropical fruits worldwide, papaya is now ranked fourth in total tropical fruit production after bananas, oranges, and mango. Global papaya production has grown significantly over the last few years, mainly as a result of increased production in India.[11] Papaya has become an important agricultural export for developing countries, where export revenues of the fruit provide a livelihood for thousands of people, especially in Asia and Latin America.

Synonyms

It is commonly known as Papaya melon tree, Pawpaw or papau, Kapaya, Lapaya, Papyas, Papye, Tapayas, Fan mu gua. Papaya plant is laticeferous as they contain specialized cells known as laticifers.

Ayurvedic Description

- **Rasa**- Katu, Tikt
- **Guna**- Laghu, Rooksha,Teekshna
- **Veerya**-Ushna,
- **Vipak**- Katu
- **Uses**- kapha vata samak, pittanasak, sothahar, badana, sthpan, dipan, pachan, vatanuloman, kafa nisark, muutral,balya

Papaya (*Carica papaya* linn)

Papaya (*Carica papaya* linn**)** is well known for its exceptional nutritional and medicinal properties throughout the world. From the times immemorial, the whole Papaya plant including its leaves, seeds, ripe and unripe fruits and their juice is used as traditional medicine. Nowadays, Papaya is considered as nutraceutical fruit due to its multifaceted medicinal properties. The prominent medicinal properties of papaya include Anti-fertility, Diuretic, Uretonic, Anti-hypertensive, Hypolipidemic, Anti-helmintic, Wound healing, Anti-fungal, Antibacterial, Antitumor and free radical scavenging activities. Phytochemically, the whole plant contains enzymes (Papain), lycopene, carotenoids, alkaloids, monoterpenoids, flavonoids, mineral and vitamins. This important nutricious fruits feed the body and immune system. In present review article, a attempt is made to compile all the strange facts available about this tasty fruit. This tasty fruit of papaya is popular among family members of all ages for the delicious dishes derived from it. Papaya, a juicy and tasty fruit, belonging to family Caricaceae is scientifically known as *Carica papaya* Linn. It is grown in various parts of the world, including India, tropical America and Europe. It is commonly known as Papaya melon tree, Pawpaw or papau, Kapaya, Lapaya, Papyas, Papye, Tapayas, Fan mu gua. Papaya plant is laticeferous as they contain specialized cells known as laticifers. Lactifiers secrete latex and dispersed throughout most plant tissues.[28] Papaya tree is basically short lived Indian tree. In the historic times, it was considered as an exotic fruit because of its buttery taste and appearance. Papaya was the first genetically modified fruit consumed by human beings for its nutritional and medicinal properties[29]

Nutritional value of papaya

The papaya is a large tree- like plant with a single stem growing from 5 to 10 m (16 to 33 ft) tall, with spirally arranged leaves confined to the trunk. The leaves are

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large, 50-70 cm in diameter, deeply palmately lobed with seven lobes. The tree is unusually un-branched, unless lopped. The flowers appear on the axils on the leaves, maturing into large fruit. The fruit is ripe when it feels soft and its skin has attained amber to orange hue.[32] Ripe and green papaya has difference in nutritional value.

Phyto-constituents of papaya

Papaya fruit is highly appreciated worldwide for its flavor, nutritional qualities and digestive properties.[32] When unripe, it contains the enzyme papain a cysteine protease with action similar to that of the pepsin in gastric juice. The latex, which contains papain, is harvested from unripe fruit by making incision in the fruit surface during a 4-5 day period and collecting the latex until it stops flowing. The greener the fruit, more active is the papain. Three other cysteine proteases have been isolated from papaya latex: chymopapain caricain and papaya protease IV.[33] These have been purified and biochemically characterized.[34]

Papain

It is belongs to the papain superfamily, as a proteolytic enzyme, papain is of critical importance in many vital biological processes in all living organisms. Papain shows extensive proteolytic activity towards proteins, short chain polypeptides, amino acid ester and amide links and is applied extensively in the fields of food and medicine. It preferentially cleaves peptide bonds involving basic amino acids[8]. Papain is a single chain globular protein with molecular weight of 23406 DA and consists of 212 amino acids with four disulphide bridges. It is stable and active under a wide range of conditions even at elevated temperatures.[35]

Hypolipidemic activity

Hydro alcoholic extract of *C. papaya* at the dose of 400 mg/kg b.w. showed reduced levels of plasma cholesterol and triglycerides along with reduced levels of plasma glucose. This evidences showing that *C. papaya* has capability to reduce the level of glucose, plasma cholesterol and triglycerides. The similar results were shown in experimentally alloxan induced diabetic rats (Gaamoussi et al., 2010). These biological activity might be shown due to the presence of phytoconstituents i.e. flavonoids, alkaloids and tannins (Satyanarayana et al., 2001). There is a strong link between diabetes mellitus, dyslipidemia, obesity and hypertension. Further scientific evaluation is required to develop its molecular level of action. Wilson et al. 2002 A compound present in crushed papaya seed that is believed to have activity against helminthic intestinal parasites, benzyl is othiocyanate (BITC –derived from benzylglucosinolate), has been shown to have an effect on vascularcontraction using a canine carotid artery in vitro model. Other studies have suggested possible purgative effects of root extracts and antihypertensive activity of fruit extracts. The present invention shows for the first time that cow urine with herbal combination or fresh juice of herbal combination is useful for treating of hyperlipidemia and obesity in mammals. An object of the present invention shows for the first time that cow urine with herbal combination or fresh juice of herbal combination or a pharmaceutically acceptable for the manufacture of medicament or nutritional supplement useful for treating Hyperlipidemia and obesity in a mammal.

Preparation of the extracts (*Carica papaya*)

The fresh leaves of *Carica papaya* was cutted into small pieces, shade dried and coarsely powdered. A known amount (20g) of the coarse powder was packed in a clean dry soxhlet apparatus. The packed material was extracted with water and ethanol in a 1:1 ratio to obtain hydroalcoholic extract. The completion of extraction was determined by the absence of colours in the side arm of soxhlet apparatus by testing the siphoned solution for absence of any residue on evaporation to dryness. The extract obtained was collected in dry and previously weighed china disk. The solvent was evaporated to dryness on a water bath. After drying the china disk was re-weighed. This procedure was repeated five times to obtained sufficient amount of the extract and yield was calculated as given below.

Weight of china disk= 57.550 gm

Weight of china disk with extract =64.378 gm

Weight of coarse powder to be taken for extraction=20 gm

$$\% \text{ Yield} = \frac{\text{Weight of china disk with extract- Weight of china disk}}{\text{Weight of coarse powder to be taken for extraction}} \times 100$$

% Yield = (64.378-57.550)*100/20

= 34.14 % w/w

Preparation of leaves juice

The fresh leaf juice of the *Carica papaya leaves* was obtained by crushing the fresh leaves in the mixer. The crushed leaves was then filtered through muslin cloth and further used for study.

Cow Urine Therapy

Cow is a mobile dispensary. It is the treasure of medicines. The cow urine therapy is capable of curing several curable and incurable diseases. The holy texts, like Atharva Veda, Charak Samhita, Rajni Ghuntu, Vridhabhagabhatt, Amritasagar, Bhavprakash, Sushrut Samhita contain beautiful description about these things. Cow Urine Treatment and Research Center, Indore has conducted a lot of research in the past few years on patients directly and claimed that it is capable of curing diabetes, blood pressure, asthma, psoriasis, eczema, heart attack, blockage in arteries, fits, cancer, AIDS, piles, prostrate, arthritis, migraine, thyroid, ulcer, acidity, constipation, gynecological problems, ear and nose problems, abortion and several other diseases. Cow urine

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has a unique place in Ayurveda and has been described in "sushrita samhita" and a ashtanga sangraha to be the most effective substance/secretion of animal origin with innumerable therapeutic value. It has been recognized as water of life or amrita. This kind of alternative treatment as panchgavya therapy or cowpathy has been reported to be beneficial even for dreaded disease like cancer, AIDS, and diabetes. Improvement has been shown or reported with those suffering from flu, allergies, colds, rheumatoids arthritis, bacterial/viral infection, tuberculosis, chicken pox, hepatitis, leucorrhuea, leprosy, ulcer, heart disease, asthma, skin infection, aging, chemical intoxication. Through extensive research studies of cow urine distillated fraction popularly known as ark has been identified as bio enhancer of the activity of commonly used antibiotic, antifungal and anticancer drug. Cow urine enhances the immune competence and improve general health of an individual prevent the free radicals formation and act as anti-aging factor reduce apoptosis in lymphocytes and help them to survive and efficiently repair the damaged DNA and this is effective for cancer therapy. The analysis of cow urine has shown that it contains nitrogen, sulphur, phosphate, sodium, manganese, carbolic acid, iron, silicon, chlorine, magnesium, malic, citric, tartaric and succinic acid, calcium salts, Vitamin A, B, C, D, E, minerals, lactose, enzymes, creatinine, hormones and gold. A person falls ill when there is deficiency or excess of the substances inside the body. The cow urine contains those substances, which are present in the human body. Therefore consumption of cow urine maintains the balance of these substances and cures incurable diseases.

Collection of Cow urine and its preperations.

The cow urine was collected from Kanhiya Gau shala, Pal Road, Jodhpur and cow urine preparations also collected from there.

Cow urine and its preparations.

Fresh cow urine: Fresh cow urine was collected in the morning, daily from kanhiya Gau shala, Pal Road, Jodhpur

Distillate cow urine (gau arc): Gau arc was prepared by distillation process. Cow urine was boiled in an iron pot to which a vapour condensing device was attached. The vapour through tube was collected in a pot put over cold water.

Residue of cow urine (ganavati):

This was residue of cow urine after distillation process. Deep iron pan was used and boiled cow urine till it become concentrated and salts remained. When the cow urine was concentrated remove it from fire and let it cool.

CONCLUSION

Hyperlipidemia is a major cause of cardiovascular disorder. At present, the treatment of hyperlipidemia mainly involves a sustained reduction in lipid level by the use of niacin, bile acid sequestrates, fibrate, in addition to statin derivative. However, due to unwanted side effects the efficacies of these compounds are debatable and there is a demand for new compounds for the treatment of hyperlipidemia. The potency of herbal drugs is significant & they have negligible side effects than the synthetic hypolipidemic drugs. There is increasing demand by patients to use the natural products with hypolipidemic activity. Hence, all the drugs discussed in this review have exhibited significant clinical & pharmacological activity. Isolation & identification of active constituents from these plants, preparation of standardized dose & dosage regimen can play a significant role in improving the hypolipidemic action.

The results of study reveal that the juice and hydroalcoholic extract of *Lagenaria siceraria* and *Carica papaya* leaves with CU when administered to the obese & hyperlipidemic rats causes significant decrease in the body weight, Serum TC, LDL, TG and VLDL level.

In present study four preparations were taken i.e. *Lagenaria siceraria* fruit juice (LSFJ) and *Carica papaya* leaves juice (CPLJ) with CU in dose of 10 ml/kg and 20 ml/kg and hydroalcoholic extract of *Lagenaria siceraria* (LSFE) and *Carica papaya* leaves extract (CPLE) with CU in dose of 100 mg/kg and 200 mg/kg. LSFJ in dose of 20 ml/kg and LSFE in dose of 200 mg/kg showed the most significant results among other preparation in high fat diet induce obese and hyperlipidemic rats.

Interestingly LSFE and CPLE with CU (200 mg/kg; p.o.) showed more significant ($p<0.001$) reduction in body weight at 15^{th} as well as 30^{th} day of treatment as compare to standard and other groups. It also showed highly significant ($p<0.001$) reduction in TC, TG, VLDL and LDL level and increase in HDL level at 30^{th} day of treatment and these results are resemble to the standard drug. (Table No. 16, 18, 21)

LSFJ & CPLJ with CU (20ml/kg; p.o.) showed very significant reduction ($p<0.0001$) in total cholesterol and increase in HDL level at 30^{th} day of treatment as compare to standard and other groups. This is important in treatment of hypercholesterolemia particularly where low HDL is the most prevalent lipoprotein for abnormality (Table No. 17, 19)

LSFJ & CPLJ with CU (20ml/kg; p.o.) also showed the more significant reduction ($p<0.001$) in the LDL level at 15^{th} as well as 30^{th} day of treatment as compare to other groups. This is useful in the treatment of atherosclerosis because high level of TC and most importantly LDL level are the predictors of atherosclerosis and LSFE & CPLE with CU (20 ml/kg;p.o.) significantly reduced both TC and LDL level. (Table No. 17, 20)

LSFE & CPLE with CU (100mg/kg; p.o.) showed less significant results throughout the study so it means that lower dose of hydroalcholic extract of *Lagenaria siceraria and Carica papaya* is not more effective in the treatment of hyperlipidemia and hyperlipidemia.

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LSFJ & CPLJ with CU (10 ml/kg;p.o.) showed non-significant (p>0.05) results throughout the study so it means that lower dose of *Lagenaria siceraria* juice and *Carica papaya* not effective in the treatment of hyperlipidemia and obesity. Additionally the biochemical parameters such as SGOT, SGPT and CK were also studied to evaluate the side effect of the LSFE,CPLE and LSFJ,CPLJ with respect to the standard drug (ATV-10 mg/kg; p.o). Percentage increment in CK level was more significant in ATV (10 mg/kg;p.o.) treated group on the 30th day of treatment as compare to other groups. SGOT and SGPT level was decrease in LSFE, CPLE and LSFJ,CPLJ treated groups at both 15th and 30th days of treatment while in the ATV (10 mg/kg;p.o.) treated group the level of SGOT and SGPT was increase. Increased muscle enzymes (SGOT, SGPT and CK) level showed the higher incident of rhabdomyolysis in ATV (10 mg/kg; p.o.) treated group while reduction in SGOT and SGPT level and less increment in CK level in LSFJ and LSFE treated groups showed the hepato-protective property of LS fruit.(Table No 22,23,24) Finally conclude that specific dose of LSFE,CPLE and LSFJ,CPLJ can be beneficial to the patients suffering from Hyperlipidemia, hyperlipidemia and atherosclerosis without compromising with wanted but unavoidable side effects of established marketed preparation like statins. The present study helps to support the traditionally claimed antihyperlipidemia, cardioprotective and cardiotonic activity of *Lagenaria siceraria* fruits and *Carica papaya* leaf with cow urine. A future work on isolation characterization and pharmacological activity of active constituents of *Lagenaria siceraria* fruit and *Carica papaya* extract and juice is required for further beneficial exploitation which was not done in current study due to time limit of designed protocol. In conclusion, cow's urine has been proved to have good action in hypolipidemic state with less side effects. So naturally available cow's urine can serve as a good drug for people with hyperlipidemia. Where atorvastatin with cow's urine combination have given better significant (p<0.001) results than compared with single cow's urine and atorvastatin drugs.

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