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REVIEW ARTICLE

An Evidence-Based Review of Anti-Obesity and Weight Lowering Effects of *Zingiber officinale* Roscoe and *Terminalia chebula* Retz

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Abstract

Since time immemorial, the Indian medical system, particularly *Ayurveda* and *Siddha*, has prioritised prevention and health over symptoms and drugs. *Siddha*, an Indian system of medicine, originated in ancient *Thamilakam* (currently Tamil Nadu, India). The combination of *Inji* (*Zingiber officinale* Roscoe), *Sukku* (*Zingiber officinale* Roscoe) and *Kadukkai* (*Terminalia chebula* Retz) as herbal therapy with numerous chemical constituents can be considered a better pharmacological approach than consuming individual ingredients and/or chemical constituents. This review is an attempt to summarize the evidence related to the anti-obesity and weight-lowering effects of ginger and *T. chebula*. The overall view shows an anti-hyperlipidemic effect of *Zingiber officinale* and *Terminalia chebula*.

Keywords: Black Myrobalan, Ginger, *Inji*, *Kadukkai*, *Siddha*, *Sukku*

1. Introduction

Artemisia annua (also known as *Qinghao*) has been used in Traditional Chinese Medicine (TCM) for hundreds of years. Only in 2015, artemisinin was identified and recognized as an antimalarial. It led to a paradigm shift in antimalarial research and therapy. Scientifically investigating a traditional medicine that has been used for hundreds of years with the help of modern methods is only a drug rediscovery process. Similarly, exploring the Indian system of medicines will provide:

A better understanding of the nature of the multi targeted approach of the Indian system of medicines. The synergistic effects of various chemical constituents are responsible for the higher therapeutic effect of herbal formulations than their individual chemical constituents.

- Major progress has been made in the identification of New Chemical Entities (NCEs) and interesting leads based on the novel chemical structures.
- Opportunity to derive new knowledge about their mechanism of action.

With its holistic systems approach and experiential grounding, ethnopharmacological knowledge can be beneficial as a discovery engine for newer, safer, and more inexpensive drugs. There has been a surge in interest in ethnopharmacological studies of the Indian medical system[1]. Since time immemorial, the Indian medical system, particularly *Ayurveda* and *Siddha*, has prioritised prevention and health over symptoms and drugs. *Clerodendrum phlomidis* (*Agnimantha* or *Arani* or

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Thaluthalai), a well-known Indian medicinal plant used in *Ayurveda* and *Siddha* systems of medicine, has been reported to contain adrenaline (a neurotransmitter and a hormone) and L-DOPA (a precursor to dopamine)[2,3]. Scientifically exploring medicinal plants, which are still used clinically by various Indian systems of medicine practitioners, would benefit the prevention or cure of many diseases.

Siddha, an Indian system of medicine, originated in ancient *Thamilakam* (currently Tamil Nadu, India). It is based on a combination of ancient spiritual disciplines, medicinal practices, alchemy and mysticism[4]. *Siddha* classical literatures are in the Tamil language, and they are largely practiced in Tamil-speaking parts of India and abroad. Many *Siddha* practices have emphasized maintaining and regulating a normal metabolism for a healthy human life. The medicines used in such practices either increase the flow of digestive juices or stimulate the gastric reflex or enhance the liver for better assimilation of nutrients or increase the nerve tone of the entire digestive tract muscles, or all of them[5].

Siddhars were the saintly people who created the *Siddha* system of medicine. A total of 18 *Siddhars* have contributed towards the development of this medical system. *Theraiyar Siddhar* is one of the important patrons of the *Siddha* system, and his contribution is immeasurable[6]. In one of his classic literature's, he quotes an herbal therapy, as translated below:

Inji (fresh ginger rhizome) in the morning, *Sukku* (dried ginger rhizome) in the afternoon and *Kadukkai* (dried fruits of *Terminalia chebula*) in the evening, consumed for a *mandalam* (48 days), will make a crouched old man throw away the stick and walk elated[7].

The above-mentioned *Siddha* herbal therapy for 48 days is still in practice in many parts of Tamil Nadu, India. *Inji* (fresh ginger rhizome) skin is peeled, cut into pieces, pounded with water and transferred to a container. It is allowed to stand for a few minutes until the white precipitation settles down. The liquid is decanted and consumed (approximately 15 mL for an average adult human) in the morning before food. A half teaspoon (approximately 2.1 g) of *Sukku* (dried ginger rhizome) powder is consumed with hot water in the afternoon before food. A full teaspoon (approximately 4.2 g) of *Kadukkai* (dried fruits of *Terminalia chebula*) powder is consumed with warm water in the evening after food. The *Kadukkai* powder used consists of ground fruit devoid of seeds. However, the quote in the classical literature is not clear about whether the therapy is for anti-ageing or rejuvenation or a healthy metabolism. However, many practicing people have reported feeling lighter, more energetic, and having a faster metabolism as a result of the therapy. Moreover, *Zingiber officinale* and *Terminalia chebula* are traditionally and scientifically known for their weight loss effects and anti-obesity activities.

Recent research has confirmed that the therapeutic effects of individual chemical constituents are usually less than those reported in extracts or fractions of the same medicinal plant material[8]. Moreover, due to the multifaceted pathological pathways of diseases, molecules that can hit >1 biological target will offer a better pharmacological approach. The combination of *Inji*, *Sukku* and *Kadukkai* as herbal therapy with numerous chemical constituents can be considered a better pharmacological approach than consuming individual ingredients and/or chemical constituents. This review is an attempt to summarize the evidence related to the anti-obesity and weight-lowering effects of *Zingiber officinale* Roscoe and *Terminalia chebula* Retz.

2. *Inji* and *Sukku*

Ginger (*Zingiber officinale* Roscoe, Zingiberaceae) is a popular spice used all over the world. The word '*Inji*' in Tamil means 'fresh ginger rhizome' and the word '*Sukku*' in Tamil means 'dried ginger rhizome' (Figure 1). Ginger is a perennial herbaceous plant that grows annual pseudostems (1m tall) bearing narrow leaf blades. The flowers contain pale yellow petals with purple edges. Individual branches grow straight from root. The taxonomical hierarchy of ginger is shown in Table 1.

Figure 1. Fresh ginger rhizome (*Inji*) and dried ginger rhizome (*Sukku*).

Table 1. Taxonomical hierarchy of ginger

Classification	Names
Kingdom	Plantae
Clade	Tracheophytes
Clade	Angiosperms
Clade	Monocots
Clade	Commelinids
Order	Zingiberales
Family	Zingiberaceae
Genus	*Zingiber*
Species	*officinale*
Binomial Name	*Zingiber officinale* Roscoe

Its roots are commonly used in folk medicine and as a flavoring. Ginger is a common worldwide spice used for meals and/or as an herbal remedy. It is commonly used to treat catarrh, rheumatism, neurological illnesses, gingivitis, toothache, asthma, stroke, constipation, and diabetes[9]. In *Ayurveda* and *Siddha* systems of medicine, ginger is a very commonly used herbal remedy, both individually and in combinations. Some evidence suggests that ginger may have an anti-inflammatory effect and also improve digestion[10,11]. Another study found that ginger reduces body weight in obese people and increases HDL cholesterol levels[12]. Ginger is a low-toxic chemical irritant and stimulates saliva production, making swallowing easier. Ginger is generally considered safe, but when consumed in powdered form, it can cause heartburn[13].

2.1 Chemical Constituents

Gingers characteristic flavour and fragrance is due to its volatile oil (around 1-3% in fresh ginger). More than 50 components have been identified from the volatile oil. Sesquiterpenes are the primary component of the volatile oil consisting predominantly zingiberene (35%), curcumene (18%), farnesene (10%) and ß-bisabolene (Table 2). The other constituents include gingerols, shogaols, paradols and zingerone. Gingerols, a homogeneous set of phenols are primarily responsible its pungency (Figure 2). Among them, [6]-gingerol is the primary pungent compound. Shogaols, the dehydrated components of gingerols, gives the dry ginger its pungency. Numerous monoterpenes, phytosterols, vitamins, dietary fibres, minerals, proteins, and amnio acids are also reported.

Table 2. Volatile and non-volatile components of ginger

Volatile components	Non-volatile components
Sesquiterpene hydrocarbons	Gingerol
Predominantly zingiberene (35 %)	Shogaols
Farnesene (10 %)	Paradols
Curcumene (18 %)	Zingerone

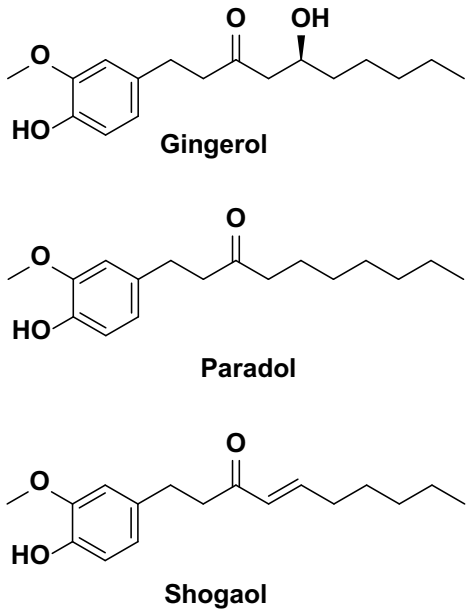

Figure 2. Chemical constituents of ginger.

A 1-3 % of the fresh ginger weight is due to the mixture of zingerone, shogaols, gingerols, and volatile oils. Fresh ginger contains zingibain, a cysteine protease enzyme[14]. Fresh ginger contains carbohydrates (18%), proteins (2%) and fats (1%). A 100 g of fresh ginger can supply energy of 80 kcal. It also contains a relatively high amount of vitamin B6 (0.16 mg) among other vitamins and magnesium (43 mg), manganese (0.229 mg) among other minerals in 100 g of ginger. Gingerols are dried to produce zingerone, a less pungent and more spicy sweet component. In higher temperatures or in acidic conditions or on long storage, shogaols, a more pungent component is produced from gingerols. Gingerol undergoes a dehydration-hydration transformation exhibiting reversible kinetics to yield its degradation product, shogaol. It was also found to be a pH dependent degradation[15]. Dried ginger contains a very negligible amount of essential nutrients and water content as compared to fresh ginger[16].

2.2 Habitat

It is a rich, lumpy, aromatic, delicate herbaceous perennial plant in the Zingiberaceae family. Native to the humid, semi damp tropical and subtropical forests of southeast Asia. It grows in a wide range of soil types, but it thrives in a warm, humid climate at elevations between 300 - 900 m. It requires well-drained soils at least 30 cm deep. Ginger requires a period of low rainfall prior to growth and evenly distributed rainfall during the growing season to survive[17].

2.3 Nutritional Profile

Table 3 represents the nutritional content of ginger rhizomes[18,19]. Table 4 represents the major ginger producing countries.

Table 3. Ginger's nutritional content (per 100 g)

Constituents	Value	Constituents	Value
Energy	80 kcal	Thiamine (B1)	0.025 mg
Carbohydrates	17.77 g	Riboflavin (B2)	0.034 mg
Sugars	1.7 g	Niacin (B3)	0.75 mg
Dietary fiber	2 g	Pantothenic acid (B5)	0.203 mg
Fat	0.75 g	Vitamin B6	0.16 mg
Protein	1.82 g	Folate (B9)	11 µg
Water	79 g	Vitamin C	5 mg
Calcium	16 mg	Vitamin E	0.26 mg
Iron	0.6 mg	Magnesium	43 mg
Manganese	0.229 mg	Phosphorus	34 mg
Sodium	13 mg	Zinc	0.34 mg

Table 4. Major ginger producing countries

No.	Country	Production (in tonnes)
1	India	1,788,000
2	Nigeria	691,239
3	China	581,137
4	Nepal	297,512
5	Indonesia	174,380
6	Thailand	166,923

3. *Kadukkai*

Kadukkai or black myrobalan or chebulic myrobalan is *Terminalia chebula* Retz. of the family Combretaceae. The word '*Kadukkai*' in Tamil means 'dried unripe fruits of *Terminalia chebula*' (Figure 3). It is native to southern Asia, ranging from India and Nepal east to southwest China (Yunnan) and south to Sri Lanka, Malaysia, and Vietnam[20,21]. The synonyms and the taxonomical hierarchy of *Terminalia chebula* are as mentioned in Tables 5 and 6.

Figure 3. *Kadukkai* - dried unripe fruits of *Terminalia chebula*.

Table 5. Synonyms of *Terminalia chebula* Retz

Buceras chebula (Retz.) Lyons	*Combretum argyrophyllum* K. Schum.
Myrobalanus chebula (Retz.) Gaertn.	*Myrobalanus gangetica* (Roxb.) Kostel.
Myrobalanus tomentella Kuntze	*Terminalia acutae* Walp.
Terminalia argyrophylla King and Prain	*Terminalia gangetica* Roxb.
Terminalia parviflora Thwaites	*Terminalia reticulata* Roth
Terminalia tomentella Kurz	*Terminalia zeylanica* Van Heurck and Mull. Arg.

Table 6. Taxonomical hierarchy of *Terminalia chebula*

Classification	Names
Kingdom	Plantae
Clade	Tracheophytes
Clade	Angiosperms
Clade	Eudicots
Clade	Rosids
Order	Myrtales
Family	Combretaceae
Genus	*Terminalia*
Species	*chebula*
Binomial Name	*Terminalia chebula* Retz.

Even though *Terminalia chebula* Retz. is considered the main black myrobalan, the different Indian systems of medicine like *Ayurveda* and *Siddha* enlist, 7 to 11 varieties for various indications. They are *Vijaya*, *Rohini*, *Putana*, *Amirtha*, *Abhya*, *Jivanti* and *Chetaki*[22]. Some reports include four more varieties, namely *Kalika*, *Pathya*, *Jaya* and *Haimavati*[23].

3.1 Chemical Constituents

Numerous glycosides, including triterpenes arjunglucoside I, arjungenin, and the chebulosides (I and II), have been isolated. Many phenolic compounds have been reported including ellagic acid, chebulinic acid, gallic acid, tannic acid, ethyl gallate, luteolin, 2,4-chebulyl-β-D-glucopyranose, punicalagin, terflavin (A and B) and terchebin[24-26]. Chebulin (a conjugated coumarin with gallic acid), chebulic and chebulinic acids have been isolated from the fruits[27,28] (Figure 4). Hydrolysable tannins are about 33% of the total chemical constituents, and they are considered to be mainly responsible for the various exhibited pharmacological activities[29,30].

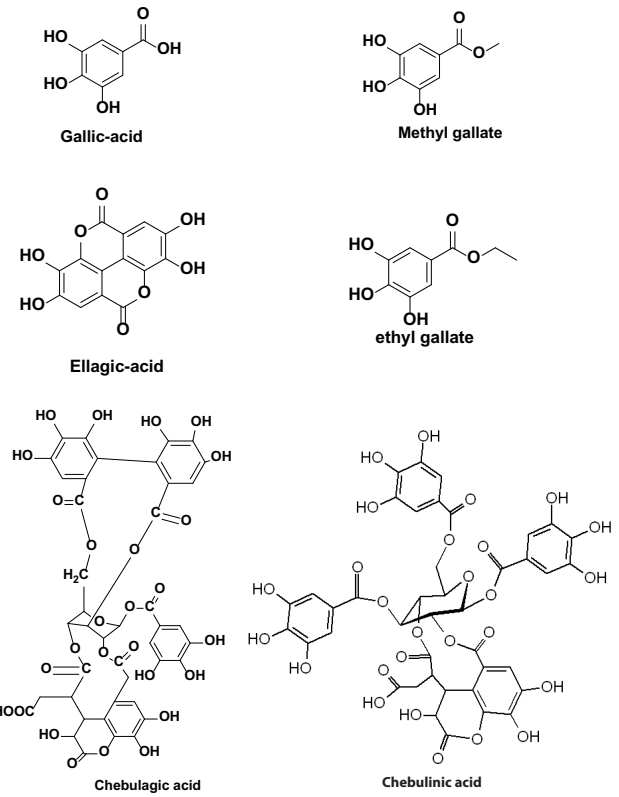

Figure 4. Chemical constituents of *Terminalia chebula*.

3.2 Habitat

It is found in India's sub-Himalayan region, stretching eastward from the Ravi River through West Bengal and Assam and climbing to 1500 m in the Himalayas. This tree is native to the forests of northern India, the central provinces and Bengal, common in Madras, Mysore and in the southern part of the Bombay Presidency. It is also widely distributed in China, Pakistan, Nepal, Bhutan, Bangladesh, Myanmar, Cambodia, Laos, Vietnam, Indonesia, Malaysia, Thailand and Sri Lanka. Its habitat includes dry slopes up to 900 m in elevation[31].

It is a medium to large deciduous tree that can reach a height of 30 m (98 ft) and has a trunk diameter of up to 1 m (3 ft 3 in). The leaves are arranged alternately to sub-oppositely, oval in shape, 7–8 cm long and 4.5–10 cm wide, with a 1–3 cm petiole[32]. They feature an acute tip, cordate at the base, complete edges, and globrous pubescence above and yellowish pubescence below. The drupe-like

fruit is 2–4.5 cm long and 1.2–2.5 cm wide, blackish, and has five longitudinal ridges[33]. Monoecious, the dull white to yellow flowers have a strong, disagreeable odour. They appear as small panicles or terminal spikes. The fruits are smooth, ellipsoid to ovoid drupes with a single angled stone, golden to orange-brown in hue.

4. Pharmacological Studies on *Zingiber officinale*

A hypolipidemic investigation conducted in a high-fat diet-induced mouse model for 12 weeks at two dosages of 250 and 500 mg/kg revealed a hypolipidemic effect[34]. Aqueous extract of ginger rhizome was administered to high-fat diet-induced rats at a dose of 20 mg/kg for 50 days; the results showed decreased body weight and increased HDL levels[35]. Ethanol extract of *Zingiber officinale* were administered to high-fat diet-induced model in rabbits at 200 mg/kg p.o for 10 weeks, it showed decreased lipid levels[36]. In another high-fat diet fed rat model, the effects of an ethanol extract of *Z. officinale* on the development of metabolic syndrome were studied at doses of 100, 200, and 400 mg/kg body weight. After 6 weeks of treatment, body weight, glucose, insulin, total cholesterol, LDL cholesterol, triglycerides, free fatty acids, and phospholipids were all decreased[37]. When alloxan-induced diabetic rats were fed ginger juice (4 mL/kg) for 10 days, lipid levels were found to be lower [38]. Ethyl acetate and ethanol extracts of *Zingiber officinale* (250 mg/kg) were administered to fructose-induced hyperlipidemic and hyperinsulinemia rats for 3 weeks. Ethanol extract was found to be more effective than ethyl acetate extract in lowering lipid levels[39]. When an aqueous extract of *Zingiber officinale* (500 mg/kg) was administered to streptozotocin and high-fat diet-induced diabetic rats for 4 weeks, it showed a hypolipidemic effect[40]. Ethanol extracts of ginger (25 µg/kg and 2500 µg/kg) were administered to high-fat diet-induced mice for 6 months, and a decrease in the levels of LDL and VLDL was observed[41]. A crude extract of *Zingiber officinal* at 200 mg/kg (6 weeks treated) showed decreased levels of cholesterol, triglycerides, LDL and increased levels of HDL in high-fat diet-fed rats[42]. *Zingiber officinale* powder (100 and 400 mg/kg) given to high-fat diet-induced rats for two weeks reduced their lipid levels[43]. In another study when a powder of *Zingiber officinale* (1 g/kg) was administered to paracetamol-induced hepatotoxicity rats for 21 days had no significant effect on hyperlipidemia[44]. Aqueous extract of *Zingiber officinale* (125 mg/kg) for 3 days in oxytetracycline-induced fatty liver rats revealed a protective effect[45]. Administration of dried ginger rhizome powder (4 g/kg) to high-fat diet-induced rabbits for 8 weeks increased HDL levels[46].

This study aimed to determine the effect of ginger on lipid and glucose levels in patients with type 2 diabetes mellitus. Ginger was found to reduce serum levels of fasting blood glucose and haemoglobin A1C in patients with type 2 diabetes in a double-blind, placebo-controlled trial involving 50 patients[47]. For 12 weeks, 80 obese women (aged 18–45 years) were randomly assigned to one of two groups: ginger or placebo (2 g/day of ginger powder or two 1 g tablets of corn starch). The study groups' body composition and adiponectin serum levels did not differ significantly. For 12 weeks, two grams of ginger powder supplementation had a minorly beneficial effect on weight loss and some metabolic characteristics of obesity[48]. For 60 days, 40 cases (either sex) were administered the combination of medications zanjabeel (*Zingiber officinale*) and amla (*Emblica officinalis*) in powder form in two divided dosages before meal. The study concluded that the tested combination of medicines has a substantial effect on lowering blood total cholesterol, serum triglycerides, serum LDL cholesterol, serum VLDL cholesterol, and boosting serum HDL cholesterol in individuals with primary hyperlipidemia[49]. Serum lipid levels were unaffected by a single intake of 10 g of ginger[50]. Zingerone showed a substantial antioxidant effect on low-density lipoproteins endothelial cells of the human aorta[51,52]. Supplementing with ginger (tablets, capsules, powder or rhizomes) the FBG and TG levels were dramatically lowered, while the HDL-C levels were significantly elevated[53]. A randomized single-blind placebo-controlled study of 100 hyperlipidemic patients, administered with ginger capsules and a placebo for 30 days, revealed that dried ginger powder at a dose of 3 g/day significantly decreased serum cholesterol levels in hyperlipidemic patients[54]. A double-blind, placebo-controlled clinical experiment conducted with hyperlipidemia individuals treated with ginger (capsule 3 gm/day in three split doses) or a control revealed a significant decrease in triglycerides, cholesterol, Very Low-Density Lipoprotein (VLDL), and Low-Density Lipoprotein (LDL). When compared to the placebo group, the results revealed that ginger has a significant lipid-lowering effect[55]. A summary is shown in Table 7.

Table 7. Summary of pre-clinical studies on *Zingiber officinale*

Animal model	Extract	Dose	Duration of treatment	Observation	References
High-fat diet-induced in mice	Aqueous and methanol extract	250 and 500 mg/kg	12 weeks	↓ lipid levels	34
High-fat diet-induced in rats	Aqueous extract	20 mg/kg	50 days	↓ body weight ↑ HDL levels	35
High-fat diet-induced in rabbits	Ethanol extract	200 mg/kg	10 weeks	↓ lipid levels	36
High-fat diet-induced in rats Ethanol extract		100, 200, 400 mg/kg	6 weeks	↓ body weight ↓ total cholesterol ↓ LDL cholesterol ↓ triglycerides ↓ free fatty acids ↓ phospholipids	37
Alloxan induced diabetic rats	Ginger juice	4 mL/kg	10 days	↓ lipid levels	38
Fructose induced hyperlipidemia and hyperinsulinemia in rats	Ethyl acetate and ethanol extract	250 mg/kg	3 weeks	Ethanol extract more effectively ↓ lipid levels	39
Streptozotocin and high-fat diet-induced diabetic rats	Aqueous extract	500 mg/kg	4 weeks	Hypolipidemic effect	40
High-fat diet-induced in mice	Ethanol extract	25 and 2500 µg/kg	6 months	↓ levels of LDL and VLDL	41
High fat diet rats	Crude extract	200 mg / kg	6 weeks	↓ levels of cholesterol ↓ levels of triglyceride ↓ levels of LDL ↑ levels of HDL	42
High-fat diet-induced rats	Powder	100 and 400 mg/kg	2 weeks	↓ lipid levels	43
Paracetamol induced hepatotoxic rats	Powder	1 g/kg	21 days	No significant effect on lipid levels	44
Oxytetracycline induced fatty liver in rats	Powder	125 mg/kg	3 days	Protective effect against fatty liver	45
High-fat diet-induced rabbits	Powder	4 g/kg	8 weeks	↑ levels of HDL	46

5. Pharmacological Studies on *Terminalia chebula*

In an atherogenic diet induced hyperlipidemia rats receiving *Haritaki* (*Terminalia chebula*) therapy demonstrated significant reductions in total cholesterol, triglycerides, total protein, and elevation of high-density lipoprotein cholesterol. The findings also suggested that *Terminalia chebula* had a lipid lowering effect at concentrations of 1.05 and 2.10 mg/kg body weight[56]. Wistar rats weighing 150–180 mg/kg when fed with high-fructose meals *ad libitum* for three weeks and followed by *T. chebula* extract at 50, 100, and 200 mg/kg orally on a daily basis showed decreased fasting blood glucose in comparison to pioglitazone at a dose of 2.7%[57]. Hydro ethanol extract (857, 642, 1714 mg/kg) was administered for 28 days to streptozotocin-induced hyperlipidemic rats and demonstrated lipid lowering effects[58]. *T. chebula* powder (25 mg/100 g bwt) given to high-fat

diet-induced rats for three weeks reduced lipid levels[59]. *T. chebula* fruit extract (200, 400, 800 mg/kg) showed a lipid-lowering effect in diazone-induced rats after 15 days[60]. Aqueous fruit extract of *T. chebula* in a polyherbal formulation (5 % in combination formulation on 100, 200, 400 mg/kg) to high-fat diet-induced rats for 2 weeks showed lipid-lowering effect[61]. In rats, *T. chebula* methanol extract showed dose-dependent anti-hyperlipidemic efficacy against hyperlipidemia produced by a high-fat diet. In a high-cholesterol diet-induced hyperlipidemic rat study, extract administered at a dose of 600 mg/kg produced effective anti-hyperlipidemic activity. It also showed a significant decrease in blood glucose level[62]. A summary is shown in Table 8.

Table 8. Summary of pre-clinical studies on *Terminalia chebula*

Animal model	Extract	Dose	Duration of treatment	Observation	References
High-fat diet-induced rats	Powder dissolved in 9 ml saline	1.05 and 2.10 mg/kg	14 days	↓ lipid levels	56
High fructose diet	Powder	50, 100, 200 mg / kg	20 days	↓ fasting blood glucose	57
Streptozotocin induced hyperlipidemia in rats	Hydro ethanolic extract	857, 642, 1714 mg/kg	28 days	↓ lipid levels	58
High fat diet in rats	Powder	25 mg/100 g b.wt.	3 weeks	↓ lipid levels	59
Diazone induced rats	Fruit extract	200, 400, 800 mg/kg	15 days	↓ lipid levels	60
High-fat diet-induced rats	Aqueous fruit extract	5 % in combination formulation of 100, 200, 400 mg/kg	2 weeks	↓ lipid levels	61
High-fat diet-induced rats	Aqueous extract	200, 400, and 600 mg/kg p.o	4 weeks	Antihyperlipidemic effect	62

6. Conclusion

The present review was sought to document the publications that have appeared on *Zingiber officinale* and *Terminalia chebula* for their metabolic effects. It has information about the preclinical and clinical trials of either individuals or drugs used in combination with other drugs. The overall review shows an anti-hyperlipidemic effect of *Zingiber officinale* and *Terminalia chebula*.

7. Acknowledgement

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