Bulletin of Pure and Applied Sciences
Vol.40A (Zoology), No.1,
January-June 2020: P.116-126

Print version ISSN 0970 0765
Online version ISSN 2320 3188
DOI 10.5958/2320-3188.2021.00015.2

Content Available online at: https://www.bpasjournals.com/zoology

Original Research Article

Antioxidant and Antihyperglycemic Potential of *Luffa acutangula* Fruit Extract in Streptozotocin-induced Diabetic Rats

[1]Rajarajan Thatchinamoorthi*, [2]Kumar Ganesan, [3]Moses Rajasekara Pandian

Author's Affiliation:
[1]Post Graduate and Research Department of Biotechnology & Microbiology, National College (Autonomous), Tiruchirappalli, Tamilnadu620001, India
[2] School of Chinese Medicine, LKS Faculty of Medicine, The University of Hong Kong, Sassoon Road, Hong Kong, China.
[3]Department of Zoology, Arignar Anna Government Arts College, Namakkal. Tamilnadu637001, India.

***Corresponding author:**
Dr. Rajarajan Thatchinamoorthi,
Assistant Professor, PG Research Department of Biotechnology &Microbiology, National College (Autonomous), Tiruchirappalli, Tamilnadu620 001, India.

E-mail: biorajarajan@gmail.com

Article Info:
Received on 11.01.2021
Accepted on 29.04.2021
Published on 15.06.2021

ABSTRACT:
Our earlier study demonstrates that the treatment of acrude extract of *Luffaacutangula* (L.) Roxb. (Family: Cucurbitaceae), a folkloric hypoglycaemic plant widely used in the southern part of India which reduces glucose level in blood under high glucose load, and in STZ-provoked diabetes in rats. This study was carried out to establish the antioxidant effects of crude extracts of *L. acutangula* (50 and 100 mg/kg) in STZ-provoked diabetic animals. Regular treatment of the fruit extracts of *L. acutangula* (50 and 100 mg/kg) for 28 days ensued noteworthy decrease in the levels of plasma TBARS, hydroperoxide, and ceruloplasmin and a substantial increase in plasma GSH, vitamins C and α-tocopherol.Based on the findings, *L. acutangula*is potential antihyperglycemic agents and restored all the antioxidant factors close to normal range. Thus, our outcomes open new prospects for advanced studies, including, a clinically based study to appraise the antidiabetic potential of the herbs.

Keywords: *Luffaacutangula,* Streptozotocin, Antioxidant Enzymes, Antidiabetic Effect.

INTRODUCTION

Diabetes is a chronic metabolic syndrome, described by a complex and heterogeneous etiology, with greater risk factors at the levels of social, behavioral, environmental, and genetic predisposition (Ganesan Xu, 2019; Thatchinamoorthi et al., 2021). It is linked to serious impacts, which severely impair peoples' quality of life and is attributed to several life-threatening problems. However, the early diagnosis and initiation of the treatment may avert or impede the onset of long-term impediments.

How to cite this article: Thatchinamoorthi R, Ganesan K, Pandian MR (2021). Antioxidant and Antihyperglycemic Potential of *Luffa acutangula*Fruit Extract in Streptozotocin-induced Diabetic Rats. *Bulletin of Pure and Applied Sciences-Zoology,* 40A(1), 116-126.

It is projected to be an extremely widespread non-communicable disease by 2025 (Ganesan et al., 2018a).In the Indian traditional medicine, many herbs are employed as antidiabetics. In practice, it is well established that the traditional system of medicine is an alternative strategy to contemporary medicine (Jayachandran et al., 2018). According to the World Health Organization, the practice of herbal medicine is required to be helpful, particularly in nations where the modern therapy of diabetes is not satisfactory (Zhang et al., 2018, 2020).

Nowadays several studies have been attention on oxidative stress, which triggers various diseases including, diabetes mellitus from the inequality between free radical generation and systems of radical hunting components (Ganesan et al., 2020a; Kumar et al., 2006; Kumar et al., 2009). In diabetes, glucose toxicity, auto-oxidation, and protein glycationmay produce enormous amounts of free radicals, resulting in lipid peroxidation (Ganesan et al., 2018b; Ganesan et al., 2017; Ganesan and Xu, 2017a).

Recent investigations have demonstrated the increased lipid peroxidation in various diabetic animal models (Ganesan et al., 2013; Ganesan et al., 2020b; Sharmila Banu et al., 2007), impaired the metabolism of glutathione (Sukalingam et al., 2018), and reduced ascorbic acid level (Ganesan et al., 2006; Ganesan et al., 2007d). The quantities of lipid peroxidation in the cell are generally defense by several cellular functions viz., enzymatic, and non-enzymatic scavenging mechanisms (Ganesan and Xu, 2017c, d). The effectiveness of these defense mechanisms is distorted during diabetes and other disease conditions(Ganesan and Xu, 2017b, e)indicating that inadequate free radical scavenging may perform important functions resulting in various tissue damages (Ganesan et al., 2008b; Ganesan et al., 2007c).Type 2 diabetes is nowadays assertive with a high rate of 3-4 new incidents every 10 seconds and is being diagnosed at a younger age of the adolescents (Ganesan et al., 2007e). The intake of exogenous insulin is greatly recognized as the safest choice of prescription for therapy in a diabetic individual. However, the linked mission and their effect particularly on insulin resistance people in DM are still inadequate.

Luffa acutangula (L.) Roxb. (family: Cucurbitaceae) has been extensively used by various populations in India, South Asia and various parts of the world for therapy of several ailments, including, diabetes, bacterial and fungal infections, dysentery, headache, renal stone, leprosy, and ringworm infection. Various experimental studies have also shown that the crude extracts of *L. acutangula* exhibited potent antioxidant (Sulaiman et al., 2013), hepato protective (Jadhav et al., 2010; Ulaganathan et al., 2010), gastro protective (Pimple et al., 2012), cardio and nephro protective (Jadhav et al., 2013), antihyperglycemic and antihyperlipidemic (Sharmin et al., 2012), antidiabetic (Raj et al., 2012) anticancer (Shendge and Belemkar, 2018; Vanajothi et al., 2012), analgesic (Quanico et al., 2008), anti-inflammatory (Gill et al., 2011), antibacterial (Nallappan, 2016), anthelmintic (Rahman, 2014), antimicrobial (Hunashal and D., 2012), and CNS depressant (Misar et al., 2004).

Phytochemical analyses have also been screened and detected around 50 compounds, including alkaloids, flavonoids, triterpene, anthraquinones, proteins, saponins, volatile compounds, and other active phytoconstituents (Jun-kai, 2002; Nagarajaiah and Prakash, 2015; Shendge and Belemkar, 2018). Our preliminary study outcome was greatly promising as it showed the glucose levels in blood, which was significantly reduced after treatment of crude fruit extracts of *L. acutangula*in normal, and high glucose load situations and STZ-provoked diabetes in rats. To our understanding, inadequate studies have been undertaken to emphasize on the antioxidant potential of *L. acutangula* fruit extract and thus this study describes the antidiabetic effect of *Luffaacutangula* and examines the impact of the test agent on blood antioxidants.

MATERIALS AND METHODS

Plant materials

The fruit of *L.acutangula* was obtained from the neighboring market in Namakkal, Tamilnadu, India, and authenticated by a taxonomist, and the Voucher Herbarium specimens were kept in the Rapinat Herbarium, Tiruchirappalli, Tamilnadu for future references. The dried raw fruits of *L.acutangula* (1Kg) were skinned, cleaned, cut into tiny pieces, and stirred in warring mixer using distilled water (2 liters). The extraction of the fruits was undertaken at a room temperature (26 ± 1^{0}C) with continual stirring during the night. The obtained homogenate was percolated using cheesecloth and spined at 4000 rpm for 15 min. The obtained supernatant was the tested drug(yield 21% w/w) was stored at 4^{o}C until use.

Animals

The investigation was undertaken on both sexes of Wistar albino rats (180-220g). The rats were kept in the Animal unit, Muthayammal College of Arts and Science, Namakkal. Animals were initially adapted for a week in lab environments and supplied a standard chow diet with water ad libitum. The animal studies were undertaken according to the animal guidance of the NIH (Council, 2011). The animals were distributed into 5 groups containing 6 animals each. Group I received as vehicle alone (gum acacia (2%), control. Group II served streptozotocin (STZ). Group III and IV served the crude extracts of fruit (50mg, 100mg/kg b.w, p.o) mixed in a vehicle and administered a single dose of STZ. Group V received glibenclamide (0.6mg/kg/ b.w, p.o) and administered a single dose of STZ. Initial food, water intake and body weight were measured. After end of the treatment, blood was drawn at 30m, 60m, and 90m time interval for the quantification of glucose in the plasma, and the testing was continued to examine the effect of fruit extract on antioxidant status in the plasma of STZ induced diabetic rats.

Induction of diabetes

The rats were established diabetes by the intraperitoneal administration of a STZ (60mg/kg, which was kept in citrate buffer, 0.1M, pH 4.5). After Forty-eight hours, blood was drawn, and levels of plasma glucose were examined to validate the development of diabetes. The animals with glucose levels at above 260mg/dl were used for the experiments.

Biochemical analysis

After 28 days of fruit extract treatment, the animals were sacrificed, and blood was drawn into heparinized tubes. Then, the plasma was obtained, followed by the determination of biochemical parameters: plasma glucose by glucose Oxidase method (Trinder, 1969),OGTT (du Vigneaud and Karr, 1925), plasma TBARS (Niehaus and Samuelsson, 1968), hydroperoxide (Jiang et al., 1992), ceruloplasmin (Ravin, 1961), reduced glutathione (GSH)(Beutler et al., 1963), α-tocopherol (vitamin E)(Baker et al., 1951) and ascorbic acid (vitamin C)(Roe and Kuether, 1943). The percentage of glycemic changes was determined by using the formula-

$$\text{Percentage of glycemic changes} = \frac{Gx - Go}{Go}$$

Where

G_o - initial glycemic values;

G_x- Glycemic values at x time interval (hours).

Statistical analysis

The values were shown as Mean ± SD. The data were analyzed using one way-ANOVA and group means were compared with Duncan's multiple comparison test (DMRT) with 95% confidence. For the statistical analysis, SPSS software package was used.

RESULTS

The effect of fruit extracts of *L.acutangula* (50, 100 mg/kg) in STZ diabetic rats is shown in Table 1. The plasma glucose levels in STZ induced diabetic rats was 240–260 mg/dl during fasting conditions. The initial significant decrease of blood sugar was noticed 2h after treatment of *L.acutangula* fruit extract. Similarly, a decrease in body weight was detected in STZ diabetic rats, but when the animals were administered orally with *L.acutangula* fruit extract (50,100 mg/ kg), the decrease in body weight was significantly improved(Table 2).

Table 1: Effect of fruit extracts of *L. acutangula* on blood glucose in normal and experimental groups

Groups	Treatment (g/kg b.w.)	Blood glucose (mg/dl)			
		Fasting	1h	2h	3h
I	Control	64.2 ± 5.27	66.1 ± 3.9^{a} (2.96)	65.3 ± 2.4^{a} (1.71)	64.3 ± 5.2^{a} (0.16)
II	Diabetic control	253.5 ± 9.2^{a}	249.5± 5.8^{bc} (–1.58)	246.8 ± 9.9^{b} (–2.64)	244.2 ± 6.8^{b} (–3.67)
III	Diabetic + *L. acutangula* 50	247.1 ± 8.3^{a}	242.6 ± 6.4^{b} (–1.82)	231.5 ± 9.5^{c} (–6.31)	221.5 ± 8.3^{c} (–10.36)
IV	Diabetic + *L. acutangula* 100	250.3 ± 8.8^{a}	247.9 ± 8.9^{bc} (–0.96)	224.6 ± 11.2^{cd} (–10.27)	213.8 ± 7.6^{d} (–14.58)
V	Diabetic + glibenclamide 0.6	252.4 ± 9.2^{a}	245.8 ± 9.4^{c} (–2.61)	219.6 ± 10.3^{d} (–12.96)	209.4 ± 8.4^{d} (–17.03)

Values are expressed as Means ± SD. Values in parenthesis show the percentof glycemic alteration. Values not sharing a common superscript vary significantly at $p<0.05$, Duncan's Multiple Range Test (DMRT)

Table 2: Effect of fruit extracts of *L. acutangula* on body weight changes, food, and water intake in experimental groups.

Groups	Treatment (g/kg b.w.)	Bodyweight		Bodyweight changes (g)	Food intake (g/week)	Water intake (L/week)
		Initial	Final			
I	Control	182.5 ± 5.5	221.5 ± 5.6^{a}	+ 39.0 ± 5.8	85.5 ± 5.34^{a}	4.89 ± 0.67^{a}
II	Diabetic control	185.8 ± 5.7	170.8 ± 6.8^{b}	-15.0 ± 4.8	70.4 ± 4.34^{b}	7.57 ± 0.96^{b}
III	Diabetic + *L. acutangula* 50	180.8 ± 4.8	183.3 ± 4.6^{c}	+2.5 ± 3.4	78.7 ± 4.89^{ab}	6.54 ± 0.37^{bc}
IV	Diabetic + *L. acutangula* 100	188.2 ± 3.9	185.3 ± 5.6^{c}	+2.9 ± 2.6	86.4 ± 5.34^{a}	6.51 ± 0.98^{bc}
V	Diabetic + glibenclamide 0.6	181.7 ± 3.8	187.5 ± 6.2^{c}	+5.8 ± 4.1	87.5 ± 4.58^{a}	5.94 ± 0.67^{c}

Values are expressed as Means ± SD. The values not sharing a common superscript vary significantly at $p<0.05$, Duncan's Multiple Range Test (DMRT)

Table 3confirms that changes in the levels of plasma glucose, thiobarbituric acid reactive substances, ceruloplasmin, and hydroperoxide in normal and experimental animals. All these parameters were significantly increased in experimental diabetic groups when compared to control groups. Treatment of *L.acutangula* fruit extracts (50,100 mg/ kg), or glibenclamide (standard drug, 0.6 mg/kg) induced a significant decrease in the content of plasma ceruloplasmin and hydroperoxide when compared to STZ diabetic animal groups. Table 4indicates the levels of the plasma GSH, vitamin E and vitamin C, which were considerably decreased in STZ induced diabetic rats when compared to normal animal groups, Administration of *L.acutangula* fruit extracts (50,100 mg/ kg, p.o.), or glibenclamide (0.6 mg/kg, p.o.) drastically elevated the levels of GSH, vitamin E and vitamin Cwhen compared to STZ induced diabetic animals.

Table 3: Effect of fruit extracts of *L. acutangula* on blood glucose, plasma TBARS, hydroperoxide, and ceruloplasmin in experimental groups.

Groups	Treatment (g/kgb.w.)	Blood glucose (mg/dl)		Plasma TBARS (nmol/ml)	Hydroperoxide (nmol/ml)	Ceruloplasmin (mg/dl)
		Initial	Final			
I	Control	67.34 ± 5.11	71.56 ± 5.78^{a}	2.8± 0.8^{a}	1.4± 0.6^{a}	28.3± 3.9^{a}
II	Diabetic control	259.45 ± 10.33	322.88 ± 14.12^{b}	3.5± 0.3^{b}	2.1± 0.4^{b}	43.5± 5.4^{b}
III	Diabetic + *L. acutangula* 50	248.77 ± 9.78	161.58 ± 10.44^{c}	3.2± 0.9^{bc}	2.0± 0.5^{b}	35.5± 4.9^{c}
IV	Diabetic + *L. acutangula* 100	254.14 ± 10.67	131.55 ± 9.36^{d}	2.8± 0.7^{ac}	1.5± 0.8^{a}	32.7± 4.7^{c}
V	Diabetic + glibenclamide 0.6	257.55 ± 9.84	111.86± 9.18^{e}	2.6± 0.2^{a}	1.4± 0.9^{a}	31.8± 3.8^{ac}

Values are expressed as Means ± SD. The values not sharing a common superscript vary significantly at p<0.05, Duncan's Multiple Range Test (DMRT)

Table4: Effect of fruit extracts of *L. acutangula* on blood GSH,vitamin Eandvitamin Cincontrolandexperimentalanimals.

Groups	Treatment (g/kg b.w.)	Blood GSH (mg/dl)	Vitamin E (mg/dl)	Vitamin C (mg/dl)
I	Control	28.4± 3.5^{a}	1.6± 0.85^{a}	2.4± 0.27^{a}
II	Diabetic control	20.1± 3.8^{b}	1.1± 0.37^{b}	1.6± 0.24^{b}
III	Diabetic + *L. acutangula* 50	23.2± 3.4^{c}	1.3± 0.85^{b}	2.0± 0.36^{ab}
IV	Diabetic + *L. acutangula* 100	26.2± 3.3^{a}	1.5± 0.15^{a}	2.2± 0.38^{a}
V	Diabetic + glibenclamide 0.6	28.1± 3.7^{a}	1.5± 0.19^{a}	2.3± 0.29^{a}

Values are expressed as Means ± SD. The values not sharing a common superscript vary significantly at p<0.05, Duncan's Multiple Range Test (DMRT)

DISCUSSION

Based on the hypothesis of the current investigation, it was to validate the hypoglycemic effect and to assess the antioxidant activities of *L.acutangula,* well-known vegetables on STZ induced-diabetic animals. The present outcomes indicate that the treatment of crude fruit extracts of *L.acutangula* diminishes the levels of plasma glucose in glucose-loaded and experimental animals. The standard drug, glibenclamide also note worthily enhances the glucose tolerance in normal and experimental animals. Glibenclamide is a sulphonyl urea agent, a clinically known drug that lowers the levels of blood glucose by accelerating β-cells of the Langerhans and discharge an adequate amount of insulin (Ganesan et al., 2007b; Jayachandran et al., 2019; Kumar et al., 2007). Streptozotocin-induced diabetic model and destroying β-cells of the Langerhans have previously been well

recognized. STZ is widely used for the induction of diabetes with concomitant insulin deficiency. Among rodent models of diabetes, the STZ rat was recognized as the precious tool to investigate both pathophysiological mechanisms of type II diabetes and the hypoglycemic activity of medicinal plants (Ganesan et al., 2008a, 2011; Kumar and Murugesan, 2008). In the current situation, there has been hard to determine the underlying mechanism of anti-hyperglycemic effect of *L.acutangula* fruit extracts. Nevertheless, according to the former reports, the possible mechanism of underlying antihyperglycemic effects could be made. It has been stated that administration of *L.acutangula* prevents the absorption of blood glucose from the gut(Pimple et al., 2012). It is highly possible to obstruct the absorption of intestinal glucose which could be accountable for the inhibition of hyperglycemia in high-glucose-fed rats.

Furthermore, *L. acutangula* provokes an extra-pancreatic action practicably by activating the glucose consumption in peripheral tissues or increasing the activation of glycolytic/glycogenic enzymes in peripheral tissues or diminish the production of the antagonist hormones, including, glucagon, growth hormones and cortisol, and (Ganesan and Gani, 2014; Sukalingam and Ganesan, 2015; Sukalingam et al., 2013).

Treatment of aqueous fruit extracts of *L. acutangula* (50 and 100 mg/kg, p.o.) has exhibited possible antioxidant effects in experimental animals. In the current investigation, we have noticed an escalation in the levels of hydroperoxide and TBARS, as an indicators of lipid peroxidation in the experimental animals. These findings provea high chance that the fruit extract primarily involves in the safeguard of all major tissues including, brain, pancreas, liver, and kidney, resulting in hyperglycemia. Elevated levels of plasma lipid peroxides and TBARS are mostly considered to be the result of tissue toxicity which upsurge the generation and discharge into the portal circulation(Kumar et al., 2004; Sharmila Banu et al., 2009a, b; Sukalingam et al., 2015; Sukalingam et al., 2017). The defense machinery of the antioxidant system is drastically changed during diabetes mellitus. Ceruloplasmin is an oxidase enzyme that operates to carry Cu^{2+} into the tissues, which has been involved in the chain-smashing activity with enabling to hunt most of the radicals in the cytoplasm (Kumar et al., 2005; Kumar et al., 2007). During diabetes, the level of ceruloplasmin was note worthily elevated when matched with normal control groups and this process may be due to the accelerating hunting potential on peroxide radical groups.

Ascorbic acid is an exceptional vitamin cum antioxidant, which mostly involves the scavenging actions of oxygen radicals. It has been recognized that vitamin C involves almost 25% of the complete peroxide radical scavenging antioxidant effects (Kumar et al., 2005; Kumar et al., 2007). In the current investigation, we have detected a reduced level of plasma vitamin C in the experimental diabetic animals. These reduced levels may be because of the enhanced consumption of ascorbic acid for inactivation of the ROS or reduce the level of GSH as the cytosolic GSH is necessary for the reusing of ascorbic acid(Ganesan et al., 2005; Islam et al., 2019). GSH is known to be a metabolic watchdog and a well-established marker of a healthy individual. In the present study, we detected a decreased plasma GSH in experimental diabetic animals. It shows the increased levels of glucose produce more oxygen free radicals and thus enhanced consumption of GSH. Similarly, the previous study was also reliable with the existing investigation that decreased levels of plasma GSH in experimental diabetic animals (Ganesan et al., 2020b; Jayachandran et al., 2019; Xu et al., 2020).

The well-known antioxidant in the plasma membrane is α-tocopherol, known as vitamin E, it generally breaks the cascade lipid peroxidation mechanism by countering with peroxide radicals, hence shielding the cell architecture on cell injury (Ganesan et al., 2020b; Jayachandran et al., 2019; Xu et al., 2020). The reduced level of α-tocopherol noticed in the experimental groups compared with the control groups,

which might be because of the elevated oxidative stress that associates with the reduction of antioxidants resulting in the occurrence of hyperglycemia.

In this perspective, Ganesan et al. (Ganesan et al., 2007a)described the reduced plasma α-tocopherol in experimental animals. A decrease in food intake, water intake and body weight were noted in experimental animals, however, administration of fruit extract of *L. acutangula* (50 and 100 mg/kg) improved the food intake, water consumption and body weight in the diabetic animals. This study was consistent with the earlier reports (Ganesan et al., 2013; Zhang et al., 2018, 2020).From the fruits of *L. acutangula*, numerous phytochemicals, including polyphenol, anthraquinones, alkaloids, proteins, saponins, triterpene, volatile components, fibers, and other phytoconstituents have been found and characterized. It is fascinating to mention that in many medicinal herbs, polyphenol has been described to show hypoglycemic and antioxidant effects (Ganesan and Xu, 2017a, c, d; Ganesan and Xu, 2018). However, the possible mechanism of flavonoids as the hypoglycemic and antioxidant can only be recognized after the validation of pharmacological trials.

CONCLUSION

This report confirms the hypoglycemic and antioxidant effect of fruit of *Luffa acutangula* in normal and offers antioxidant protection in diabetic experimental animals. Based on the current findings, we can recommend that aqueous fruit extract of *L. acutangula* be considered as antidiabetic agents for diabetic individuals.

ACKNOWLEDGMENT

The authors honestly acknowledge the faculty, and technical team members in the Department of Biotechnology, Muthayammal College of Arts and Science, Rasipuram, Namakkal, Tamilnadu who offered a potential assistance and support in this study.

REFERENCES

1. Baker, H., Frank, O., Angelis, B.D., Feingold, S. (1951). Plasma tocopherol in man at various times after ingesting free or acetylated tocopherol. Nutr.Rep. Int. 21: 531-536.
2. Beutler, E., Duron, O., Kelly, B.M. (1963). Improved method for the determination of blood glutathione. J. Lab. Clin. Med. 61: 882-888.
3. Council, N.R. (2011). Guide for the Care and Use of Laboratory Animals: Eighth Edition. The National Academies Press, Washington, DC.
4. du Vigneaud, V., Karr, W.G. (1925). Carbohydrate utilization: i. rate of disappearance of d-glucose from the blood. J. Biol. Chem. 66: 281-300.
5. Ganesan, K., Banu, G.S., Maheswaran, R., Rema, S., Pandian, M.R., Murugesan, A. (2007a). Effect of Plumbago zeylanica L. on blood glucose and plasma antioxidant status in STZ Diabetic Rats. J. Nat. Remed. 7: 66-71.
6. Ganesan, K., Banu, G.S., Murugesan, A.G.(2008a). Anti-diabetic activity of Helicteres isora L . Bark Extracts on Streptozotocin-induced Diabetic Rats. Int. J. Pharma. Sci. Nanotechnol. 1: 379-382.
7. Ganesan, K., Banu, G.S., Murugesan, A.G.(2011). Influence of Helicteres isora L . bark extracts on glycaemic control and renoprotective activity in streptozotocin-induced diabetic rats. Int. J. Pharma. Sci. Nanotechnol. 1: 379-382.
8. Ganesan, K., Banu, G.S., Murugesan, A., Pandian, M.R. (2007b). Antihyperglycaemic and antiperoxidative effect of Helicteres isora L. bark extracts in streptozotocin-induced diabetic rats. J. Appl. Biomed. 5, 97-104.
9. Ganesan, K., Banu, G.S., Murugesan, A.G. (2008b). Effect of Helicteres isora bark extracts on heart antioxidant status and lipid peroxidation in streptozotocin diabetic rats. J. Appl. Biomed. 6, 89-95.
10. Ganesan, K., Banu, G.S., Murugesan, A.G., Pandian, M.R. (2006). Hypoglycaemic effect of Helicteres isora bark extract in rats. J.

Ethnopharmacol. 107, 304-307.

11. Ganesan, K., Banu, G.S., Murugesan, A.G., Pandian, M.R. (2007c). Antihyperglycaemic and antiperoxidative effect of Helicteres isora L. bark extracts in streptozotocin-induced diabetic rats. J. Appl. Biomed. 5, 97-104.

12. Ganesan, K., Banu, G.S., Pandian, M.R. (2005). Evaluation of the antioxidant activity of Trianthema portulacastrum L. Indian J. Pharmacol. 37, 331-333.

13. Ganesan, K., Banu, G.S., Pandian, M.R. (2007d). Effect of Helicteres isora. bark extracts on brain antioxidant status and lipid peroxidation in streptozotocin diabetic rats. Pharma. Biol. 45, 753 - 759.

14. Ganesan, K., Chung, S.K., Vanamala, J., Xu, B. (2018a). Causal relationship between diet-induced gut microbiota changes and diabetes: A novel strategy to transplant Faecalibacterium prausnitzii in preventing diabetes. Int. J. Mol. Sci. 19, 3720.

15. Ganesan, K., Banu,G.S., Murugesan, A.G., Pandian, M.R. (2007e). Effect of Helicteres isora Bark Extract on Protein Metabolism and Marker Enzymes in Streptozotocin-Induced Diabetic Rats. Iranian J. Pharma. Res. 6, 123-129.

16. Ganesan, K., Gani, S.B. (2014). Relationship between ABO, Rh Blood Groups and Diabetes Mellitus, obesity in Namakkal town, Tamilnadu. Int. J. Adv. Pharma. Biol. Chem. 3,995-998.

17. Ganesan, K., Jayachandran, M., Xu, B., (2018b). A critical review on hepatoprotective effects of bioactive food components. Crit. Rev. Food Sci. Nutr. 58, 1165-1229.

18. Ganesan, K., Jayachandran, M., Xu, B. (2020a). Diet-Derived phytochemicals targeting colon cancer stem cells and microbiota in colorectal cancer. Int. J. Mol. Sci. 21, 3976.

19. Ganesan, K., Ramasamy, M., Gani, S.B. (2013). Antihyperlipideamic effect of Solanum trilobatum L. leaves extract on streptozotocin induced diabetic rats. Asian J. Biomed. Pharma. Sci. 3, 51-57.

20. Ganesan, K., Ramkumar, K.M., Xu, B. (2020b). Vitexin restores pancreatic β-cell function and insulin signaling through Nrf2 and NF-κB signaling pathways. Eur. J. Pharmacol. 888, 173606.

21. Ganesan, K., Sukalingam, K., Xu, B. (2017). Solanum trilobatum L. ameliorate thioacetamide-induced oxidative stress and hepatic damage in albino rats. Antioxidants (Basel), 6, 68.

22. Ganesan, K., Xu, B. (2017a). A critical review on polyphenols and health benefits of Black Soybeans. Nutrients 9, 455.

23. Ganesan, K., Xu, B. (2017b). Molecular targets of vitexin and isovitexin in cancer therapy: a critical review. Ann. N. Y. Acad. Sci. 1401, 102-113.

24. Ganesan, K., Xu, B. (2017c). Polyphenol-Rich Dry Common Beans (Phaseolus vulgaris L.) and Their Health Benefits. Int. J. Mol. Sci. 18, 2331.

25. Ganesan, K., Xu, B., (2017d). Polyphenol-Rich Lentils and Their Health Promoting Effects. Int. J. Mol. Sci. 18, 2390.

26. Ganesan, K., Xu, B. (2017e). Telomerase Inhibitors from Natural Products and Their Anticancer Potential. Int. J. Mol. Sci. 19,13.

27. Ganesan, K., Xu, B. (2018). A critical review on phytochemical profile and health promoting effects of mung bean (Vigna radiata). Food Sci. Human Wellness 7, 11-33.

28. Ganesan, K., Xu, B. (2019). Anti-Diabetic Effects and Mechanisms of Dietary Polysaccharides. Molecules 24, 2556.

29. Gill, N., Arora, R., Kumar, S. (2011). Evaluation of Antioxidant, Anti-inflammatory and Analgesic Potential of the Luffa acutangula Roxb. Var. amara. Res. J. Phytochem. 5, 201-208.

30. Hunashal, J.R.T., D., R., 2012. A Study on antimicrobial activity of extracts of Luffa acutangula var amara fruits. Int. J.Pharma.Bio Sci. 3, 678-685.

31. Islam, T., Ganesan, K., Xu, B., 2019. New Insight into mycochemical profiles and antioxidant potential of edible and medicinal mushrooms: A review. Int.J.Med.Mushrooms 21, 237-251.

32. Jadhav, V.B., Thakare, V.N., Suralkar, A.A., Deshpande, A.D., Naik, S.R. (2010). Hepatoprotective activity of Luffa acutangula against CCl4 and rifampicin induced liver toxicity in rats: a

biochemical and histopathological evaluation. Indian J. Exp. Biol. 48, 822-829.

33. Jadhav, V.B., Thakare, V.N., Suralkar, A.A., Naik, S.R. (2013). Ameliorative effect of Luffa acutangula Roxb. on doxorubicin induced cardiac and nephrotoxicity in mice. Indian J. Exp. Biol. 51, 149-156.

34. Jayachandran, M., Wu, Z., Ganesan, K., Khalid, S., Chung, S.M., Xu, B. (2019). Isoquercetin upregulates antioxidant genes, suppresses inflammatory cytokines and regulates AMPK pathway in streptozotocin-induced diabetic rats. Chem. Biol. Interact. 303, 62-69.

35. Jayachandran, M., Zhang, T., Ganesan, K., Xu, B., Chung, S.S.M. (2018). Isoquercetin ameliorates hyperglycemia and regulates key enzymes of glucose metabolism via insulin signaling pathway in streptozotocin-induced diabetic rats. Eur. J. Pharmacol. 829, 112-120.

36. Jiang, Z.Y., Hunt, J.V., Wolff, S.P. (1992). Ferrous ion oxidation in the presence of xylenol orange for detection of lipid hydroperoxide in low density lipoprotein. Anal. Biochem. 202, 384-389.

37. Jun-kai, L.,Chen Minghuang, Xie Jieming, Zhao Rong, Ye Xiaoming, Shi Xiaoli, Wang Ziren(2002). Purification and Characterization of Two Luffaculins, Ribosome-inactivating Proteins from Seeds of Luffa acutangula. Chinese J Biochem. Mol. Biol. 18, 609-613

38. Kumar, G., Banu, G.S., Kannan, V., Pandian, M.R. (2005). Antihepatotoxic effect of beta-carotene on paracetamol induced hepatic damage in rats. Indian J. Exp. Biol. 43, 351-355.

39. Kumar, G., Banu, G.S., Pandian, M.R. (2007). Biochemical activity of selenium and glutathione on country made liquor (CML) induced hepatic damage in rats. Indian J. Clin. Biochem. 22, 105-108.

40. Kumar, G., Banu, G.S., Pappa, P.V., Sundararajan, M., Pandian, M.R. (2004). Hepatoprotective activity of Trianthema portulacastrum L. against paracetamol and thioacetamide intoxication in albino rats. J. Ethnopharmacol. 92, 37-40.

41. Kumar G, Murugesan.A.G. (2007). Influence of Helicteres isora bark extracts on plasma and tissue glycoprotein components in streptozotocin diabetic rats. J. Clin. Diagn. Res. 1, 330-338.

42. Kumar, G., Murugesan, A.G. (2008). Hypolipidaemic activity of Helicteres isora L. bark extracts in streptozotocin induced diabetic rats. J. Ethnopharmacol. 116, 161-166.

43. Kumar, G., Murugesan, A.G., Rajasekara Pandian, M. (2006). Effect of Helicteres isora bark extract on blood glucose and hepatic enzymes in experimental diabetes. Pharmazie 61, 353-355.

44. Kumar, G., Sharmila Banu, G., Murugesan, A.G. (2009). Attenuation of Helicteres isora L. bark extracts on streptozotocin-induced alterations in glycogen and carbohydrate metabolism in albino rats. Hum. Exp. Toxicol. 28, 689-696.

45. Misar, A., Upadhye, A., Mujumdar, A. (2004). CNS depressant activity of ethanol extract of Luffa acutangula Var. amara C. B. Clarke. Fruits in mice. Indian J. Pharma. Sci. 66, 463-465.

46. Nagarajaiah, S.B., Prakash, J. (2015). Chemical Composition and Bioactive Potential of Dehydrated Peels of Benincasa hispida, Luffa acutangula, and Sechium edule. J. Herbs, Spices Med. Plants 21, 193 - 202.

47. Nallappan, D. (2016). Biogenic synthesis, characterization, and biological activity of silver nanoparticles from Eurycoma longifolia and Luffa acutangula.J. Chem. Pharma. Res.

48. Niehaus, W.G., Jr., Samuelsson, B. (1968). Formation of malonaldehyde from phospholipid arachidonate during microsomal lipid peroxidation. Eur. J. Biochem. 6, 126-130.

49. Pimple, B.P., Kadam, P.V., Patil, M.J. (2012). Protective effect of Luffa acutangula extracts on gastric ulceration in NIDDM rats: role of gastric mucosal glycoproteins and antioxidants. Asian Pac. J. Trop. Med. 5, 610-615.

50. Quanico, J., Amor, E.C., Perez, G. (2008). Analgesic and hypoglycemic activities of Bixa orellana, Kyllinga monocephala and Luffa acutangula.

Philippine J. Sci. 137, 69-76.

51. Rahman, M. (2014). In-vitro Evaluation of Cytotoxic and Anthelmintic Activity of Luffa acutangula, Luffa aegyptiaca and Momordica cochinchinensis. Br.J.Pharma.Res. 4, 267-277.

52. Raj, S., Mohammed, S., Kumar, S.V., SanthoshKumar, C., Debnath, S. (2012). Antidiabetic Effect of Luffa acutangula fruits and histology of organs in streptozotocin induced diabetic in rats. Res. J. Pharmacogn. Phytochem. 4, 64-69.

53. Ravin, H.A. (1961). An improved colorimetric enzymatic assay of ceruloplasmin. J. Lab. Clin. Med. 58, 161-168.

54. Roe, J.H., Kuether, C.A. (1943). The determination of ascorbic acid in whole blood and urine through the 2,4-dinitrophenylhydrazine derivative of dehydroascorbic acid. J. Biol. Chem. 147, 399-407.

55. Sharmila Banu, G., Kumar, G., Murugesan, A.G. (2009a). Effect of ethanolic leaf extract of Trianthema portulacastrum L. On aflatoxin induced hepatic damage in rats. Indian J. Clin. Biochem. 24, 414-418.

56. Sharmila Banu, G., Kumar, G., Murugesan, A.G. (2009b). Ethanolic leaves extract of Trianthema portulacastrum L. ameliorates aflatoxin B(1) induced hepatic damage in rats. Indian J. Clin. Biochem. 24, 250-256.

57. Sharmila Banu G, Kumar, G., Rajasekara Pandian M.(2007). Cholesterol-Lowering Activity of the Aqueous Fruit Extract of Trichosanthes dioica Roxb (L.) in Normal and Streptozotocin Diabetic Rats. J. Clin. Diagn. Res. 1, 561-569.

58. Sharmin, R., Khan, M.I., Akhtar, M.A., Alim, A., Islam, M.A., Anisuzzaman, A.S.M., Ahmed, M. (2012). Hypoglycemic and Hypolipidemic Effects of Cucumber, White Pumpkin and Ridge Gourd in Alloxan Induced Diabetic Rats. J. Sci. Res. 5, 161-170.

59. Shendge, P.N., Belemkar, S.(2018). Therapeutic Potential of Luffa acutangula: A Review on Its Traditional Uses, Phytochemistry, Pharmacology and Toxicological Aspects. Front. Pharmacol. 9, 1177.

60. Sukalingam, K., Ganesan, K. (2015). Rhesus Blood Groups Associated with Risk to Obesity and Diabetes Mellitus : A Report on Punjabi Population in Selangor, Malaysia. Int. J. Integr. Med. Sci. 2, 105-109.

61. Sukalingam, K., Ganesan, K., Ponnusamy, K. (2015). Pharmacological Properties of Trianthema portulacastrum L and its Therapeutic Potential as Complementary Medicine. Int. J. Pharma. Chem. Sci. 4, 269-274.

62. Sukalingam, K., Ganesan, K., Xu, B. (2017). Trianthema portulacastrum L. (giant pigweed): phytochemistry and pharmacological properties. Phytochem. Rev. 16, 461-478.

63. Sukalingam, K., Ganesan, K., Xu, B. (2018). Protective Effect of Aqueous Extract from the Leaves of Justicia tranquebariesis against Thioacetamide-Induced Oxidative Stress and Hepatic Fibrosis in Rats. Antioxidants (Basel) 7, 78.

64. Sukalingam, K., Ganesan, K., Gani, S.B. (2013). Hypoglycemic Effect of 6-Gingerol, an Active Principle of Ginger in Streptozotocin Induced Diabetic Rats. Res. Rev: J. Pharmacol. Toxicol. Stud. 1, 33-37.

65. Sulaiman, S.F., Ooi, K.L., Supriatno, (2013). Antioxidant and α-glucosidase inhibitory activities of cucurbit fruit vegetables and identification of active and major constituents from phenolic-rich extracts of Lagenaria siceraria and Sechium edule. J. Agric. Food Chem. 61, 10080-10090.

66. Thatchinamoorthi, R., Ganesan, K., Pandian, M.R. (2021). Hypoglycemic effects of Luffa acutangula (L.) Roxb. fruit extract in normal and streptozotocin-induced diabetic rats. Int. J. Pharma. Sci. Res. 12, 2282-2288.

67. Trinder, P. (1969). Determination of blood glucose using an oxidase-peroxidase system with a non-carcinogenic chromogen. J. Clin. Pathol. 22, 158-161.

68. Ulaganathan, I., Divya, D., Radha, K., Vijayakumar, T., Dhanaraju, M. (2010). Protective effect of Luffa acutangula (var) amara against carbon tetrachloride-induced hepatotoxicity in experimental rats. Res. J. Biol. Sci. 5,

615-624.

69. Vanajothi, R., Sudha, A., Manikandan, R., Rameshthangam, P., Srinivasan, P. (2012). Luffa acutangula and Lippia nodiflora leaf extract induces growth inhibitory effect through induction of apoptosis on human lung cancer cell line. Biomed. Prev. Nutr. 2, 287-293.

70. Xu, B., Ganesan, K., Mickymaray, S., Alfaiz, F.A., Thatchinamoorthi, R., Aboody, M.S.A. (2020). Immunomodulatory and antineoplastic efficacy of common spices and their connection with phenolic antioxidants.Bioactive Comp Health Dis. 3, 15-31.

71. Zhang, T., Jayachandran, M., Ganesan, K., Xu, B. (2018). Black Truffle Aqueous Extract Attenuates Oxidative Stress and Inflammation in STZ-Induced Hyperglycemic Rats via Nrf2 and NF-κB Pathways. Front. Pharmacol. 9, 1257.

72. Zhang, T., Jayachandran, M., Ganesan, K., Xu, B. (2020). The Black Truffle, Tuber melanosporum (Ascomycetes), Ameliorates Hyperglycemia and Regulates Insulin Signaling Pathway in STZ-Induced Diabetic Rats. Int. J. Med. Mushrooms 22, 1057-1066.