Bulletin of Pure and Applied Sciences
Zoology (Animal Science), Vol.42A, No.2,
July-December 2023: P.305-316

Print version ISSN 0970 0765
Online version ISSN 2320 3188
DOI: 10.48165/bpas.2023.42A.2.10

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

Effect of *Hibiscus rosa-sinensis* and Camel Milk on the Reproduction of Diabetic Male Albino Rats – A Review

[1]K. Chauhan, [2]P. Shuklan, [3]A. Raj, [4]S. Ahlawat, and [5]S. Rani*

Author's Affiliation:
[1,2,3,4]Research Scholar, Department of Zoology, M.D. University, Rohtak, Haryana, India, 124001

***Corresponding author:**
Dr. Sudesh Rani,
Associate Professor, Department of Zoology, M.D. University, Rohtak-124001, Haryana, India.
E-mail: sudeshrani.zoo@mdurohtak.ac.in, khushboo.rs.zoo@mdurohtak.ac.in

Article Info:
Received on 25.04.2023
Revised on 12.10.2023
Approved on 07.11.2023
Accepted on 16.11.2023
Published on 20.12.2023

ABSTRACT:
Diabetes mellitus is a long-term medical condition identified by high blood sugar levels. Two forms of diabetes most commonly occur. Type I diabetes occurs in children and type II diabetes is normally found in adults. Although diabetes affects the whole body's function surprisingly, it gives rise to male infertility. Diabetes causes impotency, and ejaculatory disorders and decreases libido in males. *Hibiscus rosa-sinensis* and camel milk both are known for their anti-diabetic properties. Both are able to deal with the oxidative stress caused by diabetes because of their antioxidant properties. Both have other properties like antibacterial, anti-inflammatory, antifungal, antimicrobial, antitumor, cardio-protective, hepato-protective etc. The crude extract of *Hibiscus rosa-sinensis* has insulin-secreting activity, significantly lowering the glucose level of blood in diabetic rats. Camel milk contains insulin-like protein which is also reported to positively decrease the blood sugar level.

Keywords:
Diabetes mellitus, Blood glucose, Reproduction, *Hibiscus rosa-sinensis*, Camel milk.

How to cite this article: Chauhan K., Shuklan P., Raj A., Ahlawat S., and Rani S. (2023). Effect of *Hibiscus rosa-sinensis* and Camel Milk on the Reproduction of Diabetic Male Albino Rats – A Review. *Bulletin of Pure and Applied Sciences-Zoology*, 42A (2), 305-316.

INTRODUCTION

Diabetes Mellitus (DM) is a chronic progressive disease characterized by hyperglycemia, mainly divided into three categories type I DM, type II DM and gestational DM. Type I DM occurs when beta cells are destroyed, causing insufficient insulin production by the pancreas. And when the body becomes resistant to insulin, it results in Type II DM. (Omolaoye *et al*., 2018). Gestational DM occurs during pregnancy, females become intolerant to glucose (American Diabetes Association, 2004).Other less-known forms of diabetes are monogenic diabetes (congenital method of diabetes) and diabetes occurs in patients with cystic fibrosis (Yang & Chan, 2016).Type II DM is the most prevailing form of diabetes and accounts for 90% of cases. It is also known as a lifestyle disorder because it is commonly linked with obesity and advanced age. Diet and exercise are most commonly recommended for this type of diabetes (Ansari *et al*., 2020).

In the year 2011, there were 366 million people affected by diabetes globally as per the report of

the International Diabetes Federation and by the year 2030, there will be 522 million people expected to have diabetes (Whiting *et al*., 2011). India, the United States and China have the maximum number of individuals with diabetes. (Wild *et al*., 2004).Uncontrolled diabetes could bring about numerous diseases, namely retinopathy, neuropathy, nephropathy, kidney failure, cardiovascular diseases, and male impotence (Atkinson & Maclaren, 1994).

OXIDATIVE STRESS

Diabetes mellitus affects the process of signal transduction. The most important participant in the development of diabetes and its complications is Oxidative Stress. It performs a pivotal role in all cases of diabetes mellitus. Oxidative stress was first observed in experimental diabetes in 1982 (Matkovics *et al*., 1982). Hyperglycemialeads to the generation of free radicals [mainly reactive oxygen species (ROS)], which are responsible for inducing oxidative stress (Sakuraba *et al*., 2002). Oxidative stress was reported as an important cause inthe development of many diseases including diabetes (Fig. 1). It ordinarily occurs whenthe amount of ROS generation is higher than the amount which is generally removed by the defence system. Oxidative stress contributes significantly to diabetes development and its complications in the macrovascular and microvascular systems (Pitocco *et al*., 2010). Although the precise mechanism is still unknown. When there is oxidative stress, it can cause the oxidation of DNA (Deoxyribonucleic acid), proteins, and lipids (Wei *et al*., 2009).Endothelial cells in both large and small vessels produce excess mitochondrial superoxide due to diabetes-related metabolic anomalies (Tiwari *et al*., 2013). Oxidative stress damages the cell indirectly by the activation of different pathways or signalling processes which promotes diabetic complications and insulin resistance (Giorgi *et al*., 2010). The hyperglycemic situation will activate insulin which in turn activates insulin receptors that existinskeletal muscles, adipose tissue, liver etc. This insulin signalling endorses glucose uptake and metabolism. Oxidative stress interrupts insulin signalling and leads to insulin resistance which is responsible for the development of diabetes mellitus (Zhang *et al*., 2020).Antioxidant treatment is recommended by researchers to counter this oxidative stress induced by diabetes.

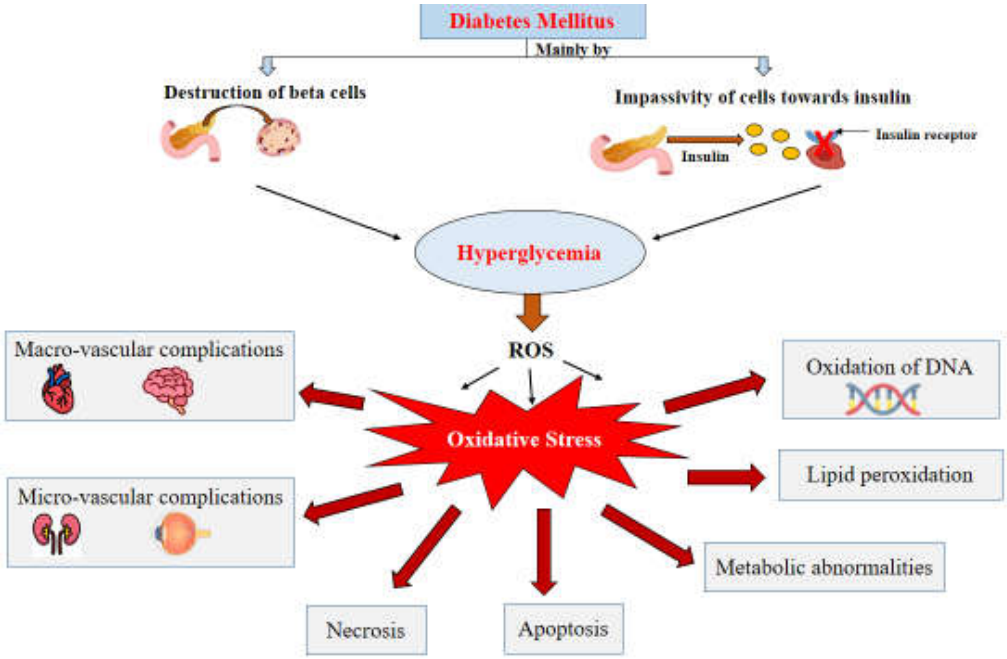

Figure 1: Diabetes and oxidative stress

THE NEGATIVE IMPACT OF DIABETES ON THE MALE REPRODUCTIVE SYSTEM

Diabetes mellitus adversely affects reproduction in both diabetic men and models of animals. It is closely associated with male infertility (Fig. 2). DM causes histological damage to the testis (Ghanbari *et al*., 2015). It also decreases sperm motility, sperm count and testosterone level (Saumya & Basha, 2017).). Sperm morphology is severely disrupted by diabetes (Rashid & Sil, 2015). There are several studies that show that diabetes alters the process of spermatogenesis (Scarano *et al*., 2006). Also, males with diabetes suffered from reduced sexual libido, impotence (Escrig *et al*., 2002), difficulties in ejaculation, hypogonadism and erectile dysfunction (Dinulovic & Radonjic, 1990). Experimental diabetic animals have decreased levels of LH, FSH, and testosterone in their serum, according to studies (Ballester *et al*., 2004). Both types of diabetes mellitus affect the function of reproductive organs in males. However, the type I form is mostly detected before reaching the age of 30 years. And type- II diabetes occurs during the reproductive phase of life (Williams & Pickup, 2004). Shrilatha (2007) observed an escalation in the DNA destruction of sperms and a decrease in the number of sperms in STZ-induced diabetic rats. DM contributes to oxidative stress in the body by generating free radicals. These free radicals alter the process of sperm maturation and cause DNA damage (Nna *et al*., 2017).

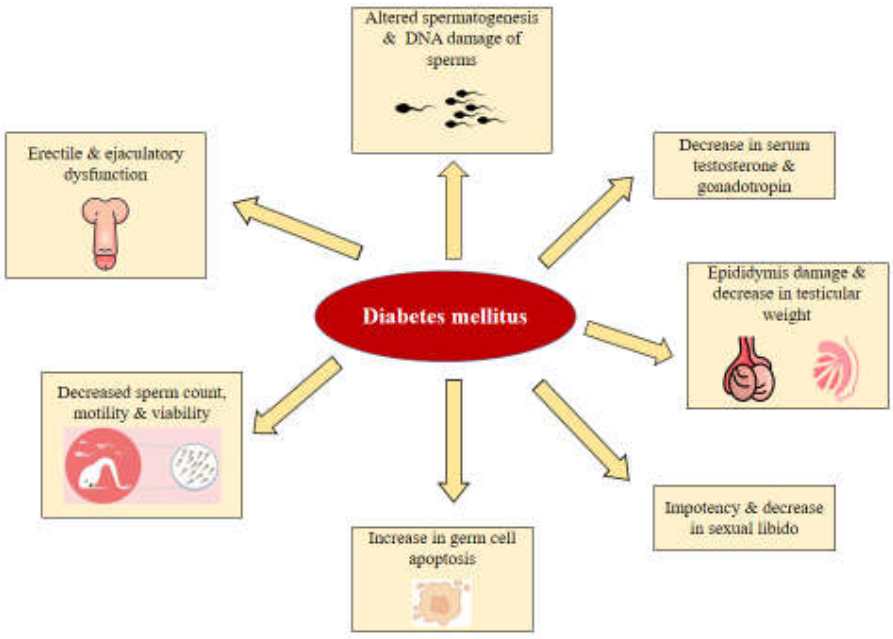

Figure 2: Effect of diabetes mellitus on the male reproductive system.

Oxidative stress caused by diabetes can result in apoptosis of spermatozoa or sperms (Kothari *et al*., 2010). Diabetes causes oxidative degradation of lipids, and disturbances in the metabolism of proteins and carbohydrates (Davis, 2006). A large number of studies were conducted on rats with diabetes induced by streptozotocin to assess its impact on their reproductive system. Vikram *et al*., (2008) observed that the dose of 45 mg per kg of body weight of streptozotocin in rats causes biochemical changes in the accessory sex organs. A further study accompanied by Navarro-Casado *et al*., (2010) where diabetic rats were treated with streptozotocin at two different doses: 45 mg/kg and 60 mg/kg of body weight. This shows the decrease in motility of sperms

and weight of testis, and epididymis also decreases. Studies reported that DM triggered changes in semen quality and decreased sperm density (Imani *et al*., 2021). And increased sperm DNA disintegration, and apoptosis of germ cells (Maresch *et al*., 2018).

Hibiscus rosa-sinensis

Diabetes mellitus is a lasting state therefore its management needs strict control of glucose levels and regular treatment to reduce the risk of diabetes-associated complications (Wong, 2005). Oral hypoglycemic drugs are commonly used to control high blood glucose levels. But these drugs have several side effects including nausea and vomiting. In Indian medicine, plants or plant-based products have been used since ancient times to treat diabetes mellitus. Because plant-based products or herbal products are less toxic and does not have any side effect like chemical drugs (Rao *et al*., 2003). The WHO also recognizes the importance of medicinal plants which have anti-diabetic properties in the effective treatment of diabetes. Many indigenous plants have been recognized in folk medicine which has anti-diabetic properties, one of them is *Hibiscus rosa-sinensis* (Jadhav *et al*., 2009). *Hibiscus rosa-sinensis* is a widely cultivated evergreen shrub for its ornamental value worldwide. It has several different colors of flower out of which the red flower variety is preferably used in traditional medicine. It comes under the Malvaceae family and it is locally called 'china rose' (Usmanghani *et al*., 1997). There are several uses of *Hibiscus rosa-sinensis* including pharmaceutical, pharmacological, cosmetical etc. It also possesses anti-cancer, anti-fungal, antioxidant and analgesic properties (Sivaraman & Saju, 2021). *Hibiscus rosa-sinensis* when compared to other species like *Hibiscus sabdariffa*c ontains more amounts of phenolics, anthocyanins, and flavonoids (Murillo Pulgarín *et al*., 2017)and these compounds play an important role in the pharmacological effects of the plant (Patel & Adhav, 2016). The Hibiscus rosa-sinensis has been traditionally used for its anti-diabetic properties in medicine. (Fig. 3). It also hasother properties like antioxidant, antitumor, anti-inflammatory, antipyretic, antifungal, antimicrobial etc (Vastrad & Byadgi, 2018). The compounds present in it are terpenoids, saponins, riboflavin, thiamine, niacin etc (Kadve *et al*., 2012). Diabetes generates free radicals causing oxidative stress. Hibiscus rosa-sinensis is rich in flavonoids and phenolic compounds, making it a potent antioxidant. Plant-derived antioxidants proved beneficial for reversing the impairment triggered by diabetes (Bhaskar *et al*., 2011).

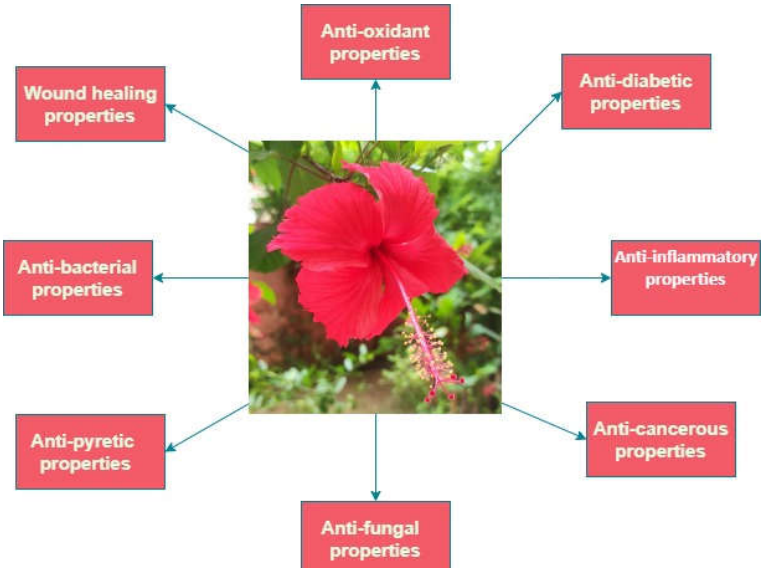

Figure 3: Different properties of *Hibiscus rosa-sinensis*

Camel milk

Camel milk is usually used in traditional medication due to its anti-diabetic properties. Camel milk is far better than bovine milk because it contains more amount of manganese, copper, zinc, and vitamins A, C and E. Therefore, camel milk has better antioxidant properties (Akbar, 2011). It does not cause any milk allergies because of the absence of β-casein and β-lactoglobulin which are the main reason for milk allergies (Fig. 4). The percentage of lactose in camel milk is lower than in the milk of other species (Al Kanhal & H. A., 2010). So, children suffering from lactose intolerance can easily digest camel milk (Shabo *et al*., 2005).When human milk is not available, camel milk can be used as a substitute. Camel milk contains an adequate amount of essential amino acids that are crucial for human health (Ho *et al*., 2021).Compared to cow milk, camel milk has significantly higher levels of insulin. Therefore, camel milk is more helpful in lowering blood glucose levels as compared to cow milk (Singh *et al*., 2006).The distinctive qualities are antimicrobial, antidiabetic and hepatoprotective properties (Althnaian *et al*., 2013).

Camel Milk 	Cow Milk 
Low lactose content	High lactose content
More protein	Less protein
Lower cholesterol	Higher cholesterol
More unsaturated fatty acids	Less unsaturated fatty acids
Less saturated fats	More saturated fats
Higher content of vitamin C, vitamin A and vitamin B	Lower content of vitamins
Not contain beta-lactoglobulin	Contains beta-lactoglobulin
Low in calories	High in calories
Not contain A1 beta-casein	Contains A1 beta-casein
High concentration of many minerals like magnesium, calcium, iron etc.	Low concentration of minerals

Figure 4: Camel milk Vs. Cow milk

Camel milk is widely used in the field of therapy because of its unique properties. It has a higher concentration of minerals including magnesium, sodium, potassium, iron, copper, and zinc but low cholesterol levels and sugar as compared to other ruminant milk (Fig. 4). Compared to cow's milk, camel milk contains greater vitamin C which boosts immunity (Yadav *et al*., 2015).

EFFECT OF *HIBISCUS ROSA-SINENSIS* ON REPRODUCTION OF DIABETIC MALE ALBINO RATS

A large number of studies reported that the extract of hibiscus used to treat inflammatory diseases, also positively affects male fertility and spermatogenesis (Reddy *et al*., 1997). Hibiscus is widely used in traditional medicine, as its extract is recognized for its anti-diabetic properties. (Ojiako *et al*., 2016). This extract significantly lowers the blood sugar level in experimental animals (Kumar *et al*., 2011). The genus *Hibiscus* has been used to treat colds since ancient times and it also has wound healing

properties. It also helps in skin rejuvenation and is used to treat damaged tissue (Shivananda Nayak *et al*., 2007). Sachdewa and Khemani observed that in diabetic experimental rats, the ethanol flower extract of *Hibiscus rosa-sinensis* significantly lowers the sugar level of blood (Sachdewa & Khemani, 2003). Its extract has tumour-suppressing properties which help in the reduction of tumour growth. Sharma *et al*., (2004) reported the anticancerous properties of *Hibiscus rosa-sinensis* in the mouse when ultraviolet radiation caused the production of tumourcells in the skin of the mouse. The antidiabetic potential of flower extract has also been observed in pregnant rats suffering from diabetes (Afiune *et al*., 2017). Venkatesh & Thilagavathi (2008) reported that in the experimental models, flower extract shows antidiabetic potential which remarkably decreases the blood glucose level. *Hibiscus rosa-sinensis* blossoms have the potential to treat diabetes along with other diseases like heart disease without producing any kind of cytotoxic effect because of the presence of antioxidants. It has an advantageous effect onmyocardial ischemic disease (Gauthaman et al., 2006). Sharma *et al*., (2016) also investigated the hypoglycemic outcome of the flowers of *Hibiscus rosa-sinensis* in type- II diabetic patients. According to Sankaran & Vadivel (2011), the *Hibiscus rosa-sinensis* flower extract has anti-oxidant and anti-diabetic properties. In rabbits also,its flower extract is recognized for its antioxidant and anti-diabetic properties (Pethe *et al*., 2017).Along with flowers, the foliage of *Hibiscus rosa-sinensis*is also known for having antidiabetic potential (Moqbel *et al*., 2011, Mamun *et al*., 2013). Its leaf extract shows insulin-secreting activity in diabetic Wistarrats (Vimala *et al*., 2008, Sachdewa *et al*., 2001).The hypoglycemic effect and antioxidant potential of the foliage of *Hibiscus rosa-sinensis* have also been calculated by Zaki *et al*., 2017.The antioxidant qualities of *Hibiscus rosa-sinensis* roots are well established and are reported to tackle diabetes-induced oxidative stress in diabetic rats (Kumar *et al*., 2013). Alam *et al*., (1990) show that in traditional medicine, rural communities use *Hibiscus rosa-sinensis* as a treatment for diabetes mellitus. Its crude extract is known for treating constipation and diarrhoea. They have also been used in healing ulcers since ancient times. Leaves and flowers are also used for promoting the growth and colour of hairs (Adhirajan *et al*., 2003). Different excerpts of *Hibiscus* show the positive effect on the diabetic male rat's reproductive system. A study by Idris *et al*., (2012) reported that the treatment of Hibiscus rosa sinensis in experimental animals with high blood sugar levels considerably amplified the number of sperms and motility. They also observed a remarkable decline in sperm abnormalities. Hibiscus extract protects testis morphology in diabetic rats, according to histological analysis. This extract reduces the oxidative destruction triggered by diabetes on the testis of diabetic rats (Budin et al., 2018). Anthocyanin, a phytopigment found in the *Hibiscus* flower has been observed to have defensive properties against testicular toxicity in rats (Amin *et al*., 2008). *Hibiscus rosa-sinensis* has been reported to provide protection against genotoxicity in Swiss albino mice because of the presence of free radical scavenging properties (Khatib *et al*., 2009).

EFFECT OF CAMEL MILK ON REPRODUCTION OF DIABETIC MALE ALBINO RATS

Camel milk is consumed in camel-rich regions to lower blood glucose levels and treat diabetes mellitus (Mohamad *et al*., 2009). In India, it was discovered that the Rajasthani population that drank camel milk had a lower incidence of diabetes than the other communities that did not (Agarwal *et al*., 2003). Drinking camel milk daily has been shown to help treat type I diabetes. (Agrawal *et al*., 2005). Nanoparticles safeguard insulin in the stomach which is present in camel milk, therefore it safely passes into the blood. Due to this reason, camel milk is able to lower the sugar level of blood (Malik *et al*., 2012). In various animal models, blood sugar levels have been observed to be reduced by camel milk. The sugar level in the bloodstream of diabetic rabbits is reduced by 78 per cent after 4-5 weeks of treatment with camel milk (EL SAID *et al*., 2010).Additionally, camel milk treatment lowers diabetic dogs' blood glucose levels by 47% (Sboui *et al*., 2010). Diabetes induces oxidative stress, camel milk contains RQ-8 peptide which is known for its antioxidant properties.

Therefore, camel milk reduces the oxidative damage caused by diabetes mellitus. Camel milk contains unique fatty acids that improve insulin sensitivity in the body and are thus able to slow down the development of type- II diabetes (Shahriari *et al*., 2018). Ebaid *et al*., (2015) concluded that camel milk improves wound healing potential and increases immunity in diabetic rats. Camel milk helps in boosting the health of diabetic patients. Clinical studies show that daily intake of camel milk by patients suffering from type I diabetes decreases the insulin requirement by 30 % and significantly lowers the glucose level of blood. This is due to insulin-like proteins present in camel milk (Agrawal *et al*., 2007).Camel milk comprises antioxidants that are helpful in regulating the glucose level of humans (Limon *et al*., 2014). Camel milk drinking has been demonstrated to increase epididymal sperm count and motility in rats. And significantly decreases sperm abnormalities. Histological study of the testis shows that camel milk improves the structure of the testis by increasing the diameter of seminiferous tubules. It raises the amount of testosterone in rats' testicles and serum (Gad *et al*., 2018). The semen characteristics are also improved by camel milk (Zakaria *et al*., 2016). Camel milk shows a protective effect on the morphology of the testis and sperms of rats (El-Azab & Elmahalaway, 2020). Mohamed *et al*., (2019) reported that camel milk effectively improves testicular and sperm damage in rats.

CONCLUSION

Diabetes mellitus is a disease that gradually worsens over time and affects millions of people worldwide. It affects the overall body functions and it also causes male infertility. Its treatment by oral drugs or chemicals has several side effects. Natural products or herbal products have been used to treat diabetes since ancient times. Both camel milk and *Hibiscus rosa-sinensis* are well acknowledged for having anti-diabetic effects. They have other properties also like antioxidants and wound healing. A large number of studies reported their hypoglycemic activity on experimental models. The extract flowers and leaves of *Hibiscus* have the insulin-secreting activity which lowers the blood glucose level. Camel milk contains insulin-like protein and therefore also reduces the blood glucose level in diabetic patients. Camel milk also increases immunity because of the presence of a high amount of vitamin C. Studies conducted on diabetic male rats show that *Hibiscus rosa-sinensis* can modify how diabetes affects the reproductive system. It significantly increases the motility, count and viability of sperm after treatment in albino rats with diabetes. Camel milk improves the morphology of the testis and also increases the level of testosterone in diabetic male albino rats. It also shows a protective effect on reproductive damage caused by insecticides or nanoparticles. So we can say that both *Hibiscus rosa-sinensis* and camel milk has significant potential to decrease blood sugar level. Also, both have antioxidant properties useful for tackling diabetes-induced oxidative stress.

Conflict of Interest

The authors declare no conflict of interest.

Acknowledgements

The authors want to thank the Department of Zoology, M. D. University, Rohtak, Haryana, India for providing suitable facilities for the work. No funding was received for the work.

REFERENCES

1. Adhirajan, N., Kumar, T. R., Shanmugasundaram, N., & Babu, M. (2003). In vivo and in vitro evaluation of hair growth potential of Hibiscus rosa-sinensis Linn. *Journal of Ethnopharmacology*, *88*(2-3), 235-239.
2. Afiune, L. A. F., Leal-Silva, T., Sinzato, Y. K., Moraes-Souza, R. Q., Soares, T. S., Campos, K. E., ... & Volpato, G. T. (2017). Beneficial effects of Hibiscus rosa-sinensis L. flower aqueous extract in pregnant rats with diabetes. *PLoS One*, *12*(6), e0179785.
3. Agarwal, R. P., Swami, S. C., Beniwal, R., Kochar, D. K., Sahani, M. S., Tuteja, F. C., & Ghouri, S. K. (2003). Effect of camel milk on glycemic control, risk factors and diabetes quality of life in type-1 diabetes: A randomized prospective controlled study. *Journal of Camel Practice and Research*, *10*(1), 45-50.

4. Agrawal, R. P., Beniwal, R., Sharma, S., Kochar, D. K., Tuteja, F. C., Ghorui, S. K., & Sahani, M. S. (2005). Effect of raw camel milk in type 1 diabetic patients: 1 year randomised study. *Journal of Camel Practice and Research*, *12*(1), 27.

5. Agrawal, R. P., Saran, S., Sharma, P., Gupta, R. P., Kochar, D. K., & Sahani, M. S. (2007). Effect of camel milk on residual beta-cell function in recent-onset type 1 diabetes. *Diabetes research and clinical practice*, *77*(3), 494-495.

6. Al Kanhal, H. A. (2010). Compositional, technological and nutritional aspects of dromedary camel milk. *International Dairy Journal*, *20*(12), 811-821.

7. Akbar, N. (2011). Science of camel and yak milk: human nutrition and health perspectives. *Food and Nutrition Sciences*, *2011*.

8. Alam, M. M., Siddiqui, M. B., & Husain, W. (1990). Treatment of diabetes through herbal drugs in rural India. *Fitoterapia*, *61*(3), 240-242.

9. Althnaian, T., Albokhadaim, I., & El-Bahr, S. M. (2013). Biochemical and histopathological study in rats intoxicated with carbon tetrachloride and treated with camel milk. *SpringerPlus*, *2*(1), 57.

10. American Diabetes Association, 2004. Diagnosis and classification of diabetes. Diabetes Care 27 (1), S5–S10.

11. Amin, A., Hamza, A. A., Kambal, A., & Daoud, S. (2008). Herbal extracts counteract cisplatin-mediated cell death in rat testis. *Asian Journal of Andrology*, *10*(2), 291-297.

12. Ansari, P., Azam, S., Hannan, J. M. A., Flatt, P. R., & Wahab, Y. H. A. (2020). The anti-hyperglycaemic activity of H. rosa-sinensis leaves is partly mediated by inhibition of carbohydrate digestion and absorption, and enhancement of insulin secretion. *Journal of Ethnopharmacology*, *253*, 112647.

13. Atkinson, M. A., & Maclaren, N. K. (1994). The pathogenesis of insulin-dependent diabetes mellitus. *New England journal of medicine*, *331*(21), 1428-1436.

14. Ballester, J., Muñoz, M. C., Domínguez, J., Rigau, T., Guinovart, J. J., & Rodríguez-Gil, J. E. (2004). Insulin-dependent diabetes affects testicular function through FSH-and LH-linked mechanisms. *Journal of andrology*, *25*(5), 706-719.

15. Bhaskar, A., Nithya, V., & Vidhya, V. G. (2011). Phytochemical screening and in vitro antioxidant activities of the ethanolic extract of Hibiscus rosa sinensis L. *Annals of Biological Research*, *2*(5), 653-661.

16. Budin, S. B., Rahman, W. Z. A., Jubaidi, F. F., Yusof, N. L. M., Taib, I. S., & Zainalabidin, S. (2018). Roselle (*Hibiscus sabdiriffa*) polyphenol-rich extract prevents testicular damage in diabetic rats. *Journal of Applied Pharmaceutical Science*, *8*(2), 65-70.

17. Davis, SN. (2006). Insulin, Oral hypoglycemic agents and the pharmacology of the endocrine pancreas. In *Goodman and Gilmans the Pharmacological Basis of Therapeutics*. Brunton LL (ed.). McGraw-Hill, New York; 1613-1645.

18. Dinulovic, D., & Radonjic, G. (1990). Diabetes mellitus/male infertility. *Archives of andrology*, *25*(3), 277-293.

19. Ebaid, H., Abdel-Salam, B., Hassan, I., Al-Tamimi, J., Metwalli, A., & Alhazza, I. (2015). Camel milk peptide improves wound healing in diabetic rats by orchestrating the redox status and immune response. *Lipids in health and disease*, *14*(1), 1-10.

20. El-Azab, N. E. E., & Elmahalaway, A. M. (2020). A Histological and Immunohistochemical Study on Testicular Changes Induced by Sliver Nanoparticles in Adult Rats and the Possible Protective Role of Camel Milk. *Egyptian Journal of Histology*, *42*(4), 1044-1058.

21. EL SAID, E. S. E. S., EL SAYED, G. R., & Tantawy, E. (2010, January). Effect of camel milk on oxidative stresses in experimentally induced diabetic rabbits. *Veterinary research forum.*

22. Escrig, A., Marin, R., Abreu, P., Luis Gonzalez-Mora, J., & Mas, M. (2002). Changes in mating behaviour, erectile function, and nitric oxide levels in penile corpora cavernosa in streptozotocin-diabetic rats. *Biology of reproduction*, *66*(1), 185-189.

23. Gad, S. B., Fayed, A. H. H., Hafez, M. H., & Abdel-Hafeiz, A. H. (2018). Does camel milk have a positive impact on rat reproductive functions? *Alexandria Journal for Veterinary Sciences*, *59*(1).

24. Gauthaman, K. K., Saleem, M. T., Thanislas, P. T., Prabhu, V. V., Krishnamoorthy, K. K., Devaraj, N. S., & Somasundaram, J. S. (2006). Cardioprotective effect of the Hibiscus rosa sinensis flowers in an oxidative stress model of myocardial ischemic reperfusion injury in the rat. *BMC Complementary and Alternative Medicine*, *6*(1), 1-8.

25. Ghanbari, E., Nejati, V., Najafi, G., Khazaei, M., & Babaei, M. (2015). Study on the effect of royal jelly on reproductive parameters in streptozotocin-induced diabetic rats. *International journal of fertility & sterility*, *9*(1), 113.

26. Giorgi, C., Agnoletto, C., Baldini, C., Bononi, A., Bonora, M., Marchi, S., & Pinton, P. (2010). Redox control of protein kinase C: cell-and disease-specific aspects. *Antioxidants & redox signalling*, *13*(7), 1051-1085.

27. Ho, T. M., Zou, Z., & Bansal, N. (2021). Camel milk: A review of its nutritional value, heat stability, and potential food products. *Food Research International*, 110870.

28. Idris, M. H. M., Budin, S. B., Osman, M., & Mohamed, J. (2012). Protective role of Hibiscus sabdariffa calyx extract against streptozotocin-induced sperm damage in diabetic rats. *Excli Journal*, *11*, 659.

29. Imani, M., Talebi, A. R., Fesahat, F., Rahiminia, T., Seifati, S. M., & Dehghanpour, F. (2021). Sperm parameters, DNA integrity, and protamine expression in patients with type II diabetes mellitus. *Journal of Obstetrics and Gynaecology*, *41*(3), 439-446.

30. Jadhav, V. M., Thorat, R. M., Kadam, V. J., & Sathe, N. S. (2009). Traditional medicinal uses of Hibiscus rosa-sinensis. *J Pharm Res*, *2*(8), 1220-1222.

31. Kadve, S., Malakar, R., Yadav, M., & Tiwari, A. (2012). Genetic variation on *Hibiscus* species by using Rapd Markers. *Advance Research in Pharmaceuticals and Biologicals*, *2*(1), 9-21.

32. Khatib, N. A., Ghoshal, G., Nayana, H., Joshi, R. K., Taranalli, A. D., NA MK, N. N., ... & RK MJ, T. A. (2009). Effect of Hibiscus rosa-sinensis extract on modifying cyclophosphamide-induced genotoxicity and scavenging free radicals in Swiss albino mice. *Pharmacologyonline*, *3*, 796-808.

33. Kothari, S., Thompson, A., Agarwal, A., & du Plessis, S. S. (2010). Free radicals: their beneficial and detrimental effects on sperm function.

34. Kumar, V., Mahdi, F., Khanna, A. K., Singh, R., Chander, R., Saxena, J. K., & Singh, R. K. (2013). Antidyslipidemic and antioxidant activities of Hibiscus rosa sinensis root extract in alloxan-induced diabetic rats. *Indian Journal of Clinical Biochemistry*, *28*(1), 46-50.

35. Limon, A., Gallegos-Perez, J. L., Reyes-Ruiz, J. M., Aljohi, M. A., Alshanqeeti, A. S., & Miledi, R. (2014). The endogenous GABA bioactivity of camel, bovine, goat and human milks. *Food Chemistry*, *145*, 481-487.

36. Malik, A., Al-Senaidy, A., Skrzypczak-Jankun, E., & Jankun, J. (2012). A study of the anti-diabetic agents of camel milk. *International journal of molecular medicine*, *30*(3), 585-592.

37. Mamun, A., Islam, S., Alam, A. K., Rahman, M. A. A., & Rashid, M. (2013). Effects of ethanolic extract of Hibiscus rosa-sinensis leaves on alloxan-induced diabetes with dyslipidemia in rats. *Bangladesh Pharmaceutical Journal*, *16*(1), 27-31.

38. Maresch, C. C., Stute, D. C., Alves, M. G., Oliveira, P. F., de Kretser, D. M., & Linn, T. (2018). Diabetes-induced hyperglycemia impairs male reproductive function: a systematic review. *Human Reproduction Update*, *24*(1), 86-105.

39. Matkovics, B., Varga, S. I., Szabo, L., & Witas, H. (1982). The effect of diabetes on the activities of the peroxide metabolism enzymes. *Hormone and Metabolic Research*, *14*(02), 77-79.

40. Mohamad, R. H., Zekry, Z. K., Al-Mehdar, H. A., Salama, O., El-Shaieb, S. E., El-Basmy, A. A., ... & Sharawy, S. M. (2009). Camel milk as an adjuvant therapy for the treatment of type 1 diabetes: verification of a traditional ethnomedical practice. *Journal of medicinal food*, *12*(2), 461-465.

41. Mohamed, A. A. R., Abdellatief, S. A., Khater, S. I., Ali, H., & Al-Gabri, N. A. (2019). Fenpropathrin induces testicular damage, apoptosis, and genomic DNA

damage in adult rats: Protective role of camel milk. *Ecotoxicology and environmental safety*, *181*, 548-558.

42. Moqbel, F. S., Naik, P. R., Najma, H. M., & Selvaraj, S. (2011). Antidiabetic properties of Hibiscus rosa sinensis L. leaf extract fractions on non-obese diabetic (NOD) mouse.

43. Murillo Pulgarín, J. A., Garcia Bermejo, L. F., & Carrasquero Durán, A. (2017). Determination of the antioxidant activity of hibiscus flowers by flow injection analysis with chemiluminescence detection. *Analytical Letters*, *50*(1), 186-196.

44. Navarro-Casado, L., Juncos-Tobarra, M. A., Chafer-Rudilla, M., De Onzono, L. Í., Blazquez-Cabrera, J. A., & Miralles-Garcia, J. M. (2010). Effect of experimental diabetes and STZ on male fertility capacity. Study in rats. *Journal of Andrology*, *31*(6), 584-592.

45. Nna, V. U., Bakar, A. B. A., & Mohamed, M. (2017). Diabetes mellitus-induced male reproductive impairment: the role of natural products: a review. *J Appl Pharm Sci*, *7*, 233-242.

46. Ojiako, O. A., Chikezie, P. C., & Ogbuji, A. C. (2016). Blood glucose level and lipid profile of alloxan-induced hyperglycemic rats treated with single and combinatorial herbal formulations. *Journal of traditional and complementary medicine*, *6*(2), 184-192.

47. Omolaoye, T. S., Skosana, B. T., & du Plessis, S. S. (2018). Diabetes mellitus-induction: Effect of different streptozotocin doses on male reproductive parameters. *Acta histochemica*, *120*(2), 103-109.

48. Patel, S., & Adhav, M. (2016). Comparative phytochemical screening of ethanolic extracts (flower and leaf) of morphotypes of Hibiscus Rosa-sinensis Linn. *Journal of Pharmacognosy and Phytochemistry*, *5*(3), 93.

49. Pethe, M., Yelwatkar, S., Gujar, V., Varma, S., & Manchalwar, S. (2017). Antidiabetic, hypolipidemic and antioxidant activities of Hibiscus rosa sinensis flower extract in alloxan-induced diabetes in rabbits. *Int J Biomed Adv Res*, *8*, 138-43.

50. Pitocco, D., Zaccardi, F., Di Stasio, E., Romitelli, F., Santini, S. A., Zuppi, C., & Ghirlanda, G. (2010). Oxidative stress, nitric oxide, and diabetes. *The review of diabetic studies: RDS*, *7*(1), 15.

51. Kumar, T. R., Kumar, E. U., Sekar, M., & Kumar, M. S. (2011). Antidiabetic activity of methanolic extract of Hibiscus cannabinus in streptozotocin-induced diabetic rats. *International Journal of Pharma and Bio Sciences*, *2*(1), P125-P130.

52. Rao, B. K., Sudarshan, P. R., Rajasekhar, M. D., Nagaraju, N., & Rao, C. A. (2003). Antidiabetic activity of Terminalia pallida fruit in alloxan-induced diabetic rats. *Journal of Ethnopharmacology*, *85*(1), 169-172.

53. Rashid, K., & Sil, P. C. (2015). Curcumin ameliorates testicular damage in diabetic rats by suppressing cellular stress-mediated mitochondria and endoplasmic reticulum-dependent apoptotic death. *Biochimica et biophysica acta (BBA)-molecular basis of disease*, *1852*(1), 70-82.

54. Reddy, C. M., Murthy, D. R., & Patil, S. B. (1997). Antispermatogenic and androgenic activities of various extracts of *Hibiscus rosasinesis* in albino mice. *Indian Journal of Experimental Biology*, *35*(11), 1170-1174.

55. Sachdewa, A., Nigam, R., & Khemani, L. D. (2001). Hypoglycemic effect of Hibiscus rosa sinensis L. leaf extract in glucose and streptozotocin-induced hyperglycemic rats.

56. Sachdewa, A., & Khemani, L. D. (2003). Effect of Hibiscus rosa sinensis Linn. Ethanol flower extract on blood glucose and lipid profile in streptozotocin-induced diabetes in rats. *Journal of Ethnopharmacology*, *89*(1), 61-66.

57. Sakuraba, H., Mizukami, H., Yagihashi, N., Wada, R., Hanyu, C., & Yagihashi, S. (2002). Reduced beta-cell mass and expression of oxidative stress-related DNA damage in the islet of Japanese Type II diabetic patients. *Diabetologia*, *45*(1), 85-96.

58. Sankaran, M., & Vadivel, A. (2011). Antioxidant and Antidiabetic effect of *Hibiscus rosa-sinensis* flower extract on Streptozotocin induced experimental rats-a dose response study. *Notulae Scientia Biologicae*, *3*(4), 13-21.

59. Saumya, S. M., & Basha, P. M. (2017). Fluoride exposure aggravates the testicular damage and sperm quality in diabetic mice: protective role of ginseng and banaba. *Biological trace element research*, *177*(2), 331-344.

60. Scarano, W. R., Messias, A. G., Oliva, S. U., Klinefelter, G. R., & Kempinas, W. G. (2006). Sexual behaviour, sperm quantity and quality after short-term streptozotocin-induced hyperglycaemia in rats. *International journal of andrology*, *29*(4), 482-488.

61. Shabo, Y., Barzel, R., Margoulis, M., & Yagil, R. (2005). Camel milk for food allergies in children. *IMAJ-RAMAT GAN-*, *7*(12), 796.

62. Shahriari, S., Hejazi, N., & Eftekhari, M. H. (2018). The role of camel milk in treatment of type 2 diabetes: a review. *International Journal of Nutrition Sciences*, *3*(3), 120-126.

63. Sharma, S., Khan, N., & Sultana, S. (2004). Effect of Onosma echioides on DMBA/croton oil mediated carcinogenic response, hyperproliferation and oxidative damage in murine skin. *Life Sciences*, *75*(20), 2391-2410.

64. Sharma, K., Pareek, A., & Chauhan, E. S. (2016). Evaluation of the hyperglycemic and hyperlipidemic mitigating impact of Hibiscus rosa-sinensis (Gudhal) flower in type II diabetes mellitus subjects. *International Journal of Applied Biology and Pharmaceutical Technology*, *7*(2), 223-228.

65. Sboui, A., Khorchani, T., Djegham, M., Agrebi, A., Elhatmi, H., & Belhadj, O. (2010). Anti-diabetic effect of camel milk in alloxan-induced diabetic dogs: a dose–response experiment. *Journal of animal physiology and animal nutrition*, *94*(4), 540-546.

66. Shivananda Nayak, B., Sivachandra Raju, S., Orette, F. A., & Chalapathi Rao, A. V. (2007). Effects of Hibiscus rosa sinensis L (Malvaceae) on wound healing activity: a preclinical study in a Sprague Dawley rat. *The international journal of lower extremity wounds*, *6*(2), 76-81.

67. Shrilatha, B. (2007). Early oxidative stress in testis and epididymal sperm in streptozotocin-induced diabetic mice: its progression and genotoxic consequences. *Reproductive Toxicology*, *23*(4), 578-587.

68. Singh, R., Ghorui, S. K., & Sahani, M. S. (2006). Camel milk: Properties and processing potential. *Sahani, MS The Indian camel. NRCC, Bikaner*, 59-73.

69. Sivaraman, C. M., & Saju, F. (2021). Medicinal value of Hibiscus rosa sinensis: A review. *International Journal of Pharmacognosy and Chemistry*, 1-11.

70. Tiwari, B. K., Pandey, K. B., Abidi, A. B., & Rizvi, S. I. (2013). Markers of oxidative stress during diabetes mellitus. *Journal of biomarkers*, *2013*.

71. Usmanghani, K., Saeed, A., & Alam, M. T. (1997). Indusyunic medicine. *Department of Pharmacognosy, Faculty of Pharmacy, University of Karachi, Pakistan*, 363-364.

72. Vastrad, J. V., & Byadgi, S. A. (2018). Phytochemical screening and antibacterial activity of Hibiscus rosa-sinensis leaf extracts. *International Journal of Current Microbiology and Applied Sciences*, *7*(3), 3329-3337.

73. Venkatesh, S., & Thilagavathi, J. (2008). Anti-diabetic activity of flowers of Hibiscus rosasinensis. *Fitoterapia*, *79*(2), 79-81.

74. Vikram, A., Tripathi, D. N., Ramarao, P., & Jena, G. B. (2008). The intervention of D-glucose ameliorates the toxicity of streptozotocin in accessory sex organs of the rat. *Toxicology and applied pharmacology*, *226*(1), 84-93.

75. Vimala, H., Naik, P. R., & Chandavar, V. R. (2008). The insulin-secreting activity of Hibiscus rosa sinensis Linn, leaf extract in diabetes-induced Wistar rat. *The Bioscan*, *3*, 293.

76. Wei, W., Liu, Q., Tan, Y., Liu, L., Li, X., & Cai, L. (2009). Oxidative stress, diabetes, and diabetic complications. *Haemoglobin*, *33*(5), 370-377.

77. Whiting, D. R., Guariguata, L., Weil, C., & Shaw, J. (2011). IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. *Diabetes research and clinical practice*, *94*(3), 311-321.

78. Wild, S., Roglic, G., Green, A., Sicree, R., & King, H. (2004). Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes care*, *27*(5), 1047-1053.

79. Williams, G., & Pickup, J. C. (2004). *Handbook of diabetes*. Blackwell Pub.

80. Wong, N. D. (2005). Intensified screening and treatment of the metabolic syndrome for cardiovascular risk reduction. *Preventive Cardiology*, *8*(1), 47-54.

81. Yadav, A. K., Kumar, R., Priyadarshini, L., & Singh, J. (2015). Composition and medicinal properties of camel milk: A Review. *Asian Journal of Dairy and Food Research*, *34*(2), 83-91.

82. Yang, Y., & Chan, L. (2016). Monogenic diabetes: what it teaches us on the common forms of type 1 and type 2 diabetes. *Endocrine Reviews*, *37*(3), 190-222.

83. Zakaria, A. D., Bayad, A. E. S., Abdel-Raheem, S. M., Al-Busadah, K. A., & Albokhadaim, I. (2016). Camel's milk improves the semen characteristic in immobilization-stressed rats. *Asian Journal of Animal Sciences*, *10*(2), 139-146.

84. Zaki, L. H., Mohamed, S. M., Bashandy, S. A., Morsy, F. A., Tawfik, K. M., & Shahat, A. A. (2017). Hypoglycemic and antioxidant effects of Hibiscus rosa-sinensis L. leaves extract on liver and kidney damage in streptozotocin-induced diabetic rats. *African Journal of Pharmacy and Pharmacology*, *11*(13), 161-169.

85. Zhang, P., Li, T., Wu, X., Nice, E. C., Huang, C., & Zhang, Y. (2020). Oxidative stress and diabetes: antioxidative strategies. *Frontiers of medicine*, *14*(5), 583-600.

****