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Antihyperglycemic Activity Of Ficus Sarmentosa Leaf Extract On Streptozotocin Induced Diabetic Rats

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ABSTRACT

Background: *Diabetes mellitus remains the global health challenge, necessitating exploration of the alternative therapy derived from medicinal plants. Ficus species have a long been used in traditional medicine for managing metabolic disorder with supported by anecdotal evidence but requiring scientific validation.* ***Aim:*** *This study aim to evaluate the anti hyperglycemic potential of Ficus sarmentosa leaf extract in Streptozotocin (STZ) induced diabetic rats and correlate its ethnomedicinal use in the experimental evidence.* ***Methodology:*** *Diabetes induced in the albino wistar rats of either male or female se via intraperitoneal injection of STZ of 60 mg/kg b.w. which dissolved in the citrate buffer of 0.01 M & pH 4.5. Post induction the rats were grouped to receive daily oral doses of petroleum ether, ethyl acetate, methanolic, or aqueous leaf extracts for 9 days, adhering to OECD guidelines for animal experimentation. Ficus sarmentosa leaf extracts in various solutions viz. petroleum ether, methanol, ethyl acetate and aqueous were administered to diabetic rats for the 9 days. The effect of extract on blood glucose and body weight was studied on day 1 and 9.* ***Results:*** *The study shows that ethyl acetate, aqueous extracts and methanolic of Ficus sarmentosa leave reduced blood glucose level & body weight significantly. Body weight loss, a hallmark of uncontrolled diabetes was mitigated by 12 to 15% in treated groups that suggesting improved metabolic stability. Petroleum ether extract exhibited negligible effects with highlighting solvent dependent bioactivity.* ***Conclusion:*** *This make justify the use of Ficus species as the ethnomedical medicine for diabetes mellitus treatment. Phyto constituents such as flavonoids or terpenoids may underlie its antihyperglycemic activity, warranting further phytochemical and mechanistic studies. These findings strengthen the rationale for integrating Ficus species into complementary antidiabetic therapies.*

Keywords : *Streptozotocin, Antihyperglycemic, Intraperitoneal, Diabetes Mellitus.*

INTRODUCTION

Medicinal plant consist of components of therapeutic values and had been used as remedies for human diseases on the grounds that long. currently, due to the pathogen resistance in opposition to the available antibiotics and the recognition of traditional medicinal drug as an alternative shape of fitness care has reopened the studies domain for the organic sports of medicinal flora [1]. Medicinal plant being as an crucial herbal useful resource

and potentially secure drugs can play an essential function in assuaging human health by using contributing herbal drugs. In the rural and far flung regions of India more than 70 percent of population relies upon on folks and conventional machine of medicines obtained from flora. The high value of allopathic remedy and their potential facet consequences, advocated the human beings to apply the traditional medicine [2].

Diabetes mellitus is a most important purpose of morbidity and mortality in human populations [3]. It's miles a syndrome characterised by using hyperglycemia, polydipsia & polyuria and causes headaches to the eyes, kidneys and nerves. It is also related to an elevated incidence of cardiovascular sickness [4]. It is the maximum common endocrine ailment, affecting approximately 16 million individuals inside the U.S.A and as many as 200 million global. Perhaps extra importantly, people with diabetes are disproportionate users of the fitness care gadget. In 1992 health care prices per person with diabetes were extra than 3 instances more than in line with capita expenditure for the ones without diabetes. Ficus is a pan tropical genus of about 850 species of woody trees, shrubs, vines, epiphytes and hemi epiphyte in the circle of relatives Moraceae. together referred to as **Fig trees** or **Figs**, they're shrubs or timber, once in a while scandent, sap milky leaves alternate, hardly ever opposite, whole, not often serrate or lobbed, stipules varous. The use of Ficus species as ethnomedicine in Nepal is quite noteworthy [5]. F. benghalensis (Bar) is maximum vital used to heal 22 illnesses. Ficus sarmentosa bark powder is taken to remedy boils and secrete greater milk all through transport. Root extract is used in malaria [6]. A initial examine in our laboratory showed decreases in blood glucose tiers and meals consumption in STZ diabetic rats given aqueous or ethanolic extracts of leaves of F. sarmentosa intraperitoneally [7]. But, no reviews are to be had approximately the constituents of those flowers that's responsible for the anti diabetic activity.

The therapeutic potential of species of Ficus goes beyond the foreground of traditional uses; indeed, an entirely different approach has arisen in recent times, seeking to determine the bioactive compounds responsible in the plant for various medicinal activities via phytochemical profiling [8]. Analysis of Ficus sarmentosa led to the investigation of flavonoids, alkaloids, tannins, and phenolic substances known to have an antioxidant, anti-inflammatory, and hypoglycemic effect [9]. These substances may be involved in anti hyperglycemic activity whether by building up insulin sensitivity or limiting intestinal glucose absorption based upon preliminary studies. Studies are ongoing to confirm the exact constituents and to determine their mechanisms of action [10]. Further, ethnomedicinal applications of Ficus species point out their wide ranging diversity applied to wound healing and combating infectious diseases [11]. Another example of vast ethnobotanical relevance of Ficus species can be exemplified by Indian traditional medicine, where decoctions of Ficus benghalensis leaves are used for digestive disorders and aerial roots for management of skin diseases [12].

In addition, to herbals derived from Ficus may join modern medicine and serve chronically threatening diseases like diabetes, especially in situations where there is a shortage of resources. Being cheap and amply available, medicinal plants could indeed be a good choice for allopathic medicines, which are quite expensive, especially in rural areas where even health infrastructure is comparatively inadequate [13]. Yet, these continue to be stumbling blocks related to standardization & clinical evidence for efficacy of herbal formulations. Collaborative forum of ethnobotanists, pharmacologists and physicians would help in the negotiating between indigenous knowledge and evidence based medicine [14]. With such support researcher may be able to apply sophisticated analytical tools, such as high performance liquid chromatography, to identify active constituents from Ficus species, which is an essential step toward the development of promising phytomedicines. Such movements enable formally recognized herbal medicine for a sustainable treatment of diabetes and other conditions [15].

MATERIALS AND METHODS

Following solvents, chemicals and reagents of analytical grade or best possible grade supplied by approved companies were used.

Solvents/Reagents Used:

Table1: List of chemicals

S. No.	Name	Supplier
1.	Chloroform	Fine Chemical Co.Ltd
2.	Methanol	Pioneer chemical co.,Delhi
3.	Ethanol	Ranbaxy Labs, NewDelhi.

4.	Petroleum Ether	QUALIGENSFINECHEMICALS
5.	Carbon tetrachloride	Pioneer chemical co.,Delhi
6.	Tween80	Merck Specialties pvt ltd
7.	Starch	SD Fine-chem limited
8.	Sodium CMC	Fine Chemical Co.Ltd
9.	Sucrose	Fine Chemical Co.Ltd
10.	Sodiumlauryl sulphate	Fine Chemical Co.Ltd
11.	Microcrystalline cellulose	Fine Chemical Co.Ltd
12.	Dexamethasone	Fine Chemical Co.Ltd

Equipments and Instruments Used: Glucometer:Wockhardt Ltd.Mumbai

Experimental Animal selection: The albino Wistar rats (male and female) weighing more than 130 gm were procured from animal house GRD(PG)-IMT, Dehradun, reared and maintained at the standard house condition, that feds with commercial feed & water ad libitum. All the housing Condition & animal handling were in accordance with CPCSEA OECD guidelines. (CPCSEA-Rgistration no.- 1145/a/07/CPCSEA/2011/6), Before performing the experiment, the ethical clearance was obtained from the Institutional Animal Ethical Committee, Department of Pharmacy, GRD (PG)-IMT, Dehradun.

Collection and Authentication: In the present study, the leaves of Ficus sarmentosa were collected from local area of District Chamoli, Uttarakhand. The plants were authenticated from Botanical Survey of India, Kaulgarh Road, Dehradun and voucher specimens were preserved at Herbarium.

Extraction of Plants: The shade dried leaves of Ficus sarmentosa were reduced to fine powder (# 40 size mesh) and around 500 g of powders were subjected to successive hot continuous extraction (Soxhlet) with petroleum ether, ethyl acetate, methanol and water. After effective extractions, the solvent was distilled of the extract were then conc. on water bath & the extract obtained with solvent was weighed. Its percentage will be calculated in terms of air dried weight of plant material. The colour and consistency of the extracts will be noted. For aqueous extract maceration was used.

Phytochemical Screening Methods:

Standard phytochemical tests were conducted for the detect presence of secondary metabolites in it :

i. **Saponins**: 300 mg of extract in 5 ml water boiled for 2 mins , cooled, shaken vigorously and observed for persistent frothing [16].

ii. **Tannins**: Extract mixed with 2% sodium chloride, filtered, then 1% gelatin added; precipitation confirmed tannins [17].

iii. **Triterpenes**: 300 mg extract in 5 ml chloroform, warmed for 25 to 30 mins, followed by addition of conc. sulfuric acid. Red coloration indicated triterpenes [18].

iv. **Alkaloids**: Extract digested with 2 M HCl, filtered, and mixed with amyl alcohol; pink color in the alcohol layer indicated alkaloids [19].

v. **Flavonoids**: Detected using 1% aluminum chloride in methanol, HCl, magnesium turnings, and KOH; red coloration confirmed presence [20].

vi. **Glycosides**: Alcoholic extract boiled with Fehling solution. Brick Red precipitate indicated glycoside [21].

Experimental Induction of Diabetes:

Following 18 hours of being without food, rats were given an STZ injection of 60 mg/kg in citrate buffer (0.01 M, pH 4.5). After 48 hours, rats with fasting glucose above 300 mg/dL were claimed to be diabetic. The group receiving control was treated with saline. We gave a 5% dextrose solution immediately after giving STZ to prevent early hypoglycemia for 24 hours. [22, 23, 24].The effects of streptozotocin is given in Fig. 2.

Acute Oral Toxicity – OECD Guideline 423 :

All acute toxicity tests were conducted under CPCSEA registration and followed OECD guideline (423). Rats (300 g) injected with extracts in water with 1% Tween 80 received doses ranging from 300 mg/kg to 5000 mg/kg. No animals died when given the highest dose in the study. A dose of 500 mg/kg was picked as the most effective.

Mortality and behavior changes in the rats were measured for the first 24 hours [25, 26].

Experimental model:
Six Albino Wistar rats (>160 g) were put into separate groups and housed under a 12-hour light and dark cycle. Nine days of treatment was given to all groups. All of the vehicle mice received only vehicle, meanwhile the other groups received extracts (500 mg/kg) or Glibenclamide (600 µg/kg) through an intra gastric tube [27]. Everyone's weight was measured on the first day, the second day and again on Day 4 and Day 9.

Table 2 : Experimental protocol.

Group	Diabetic animals	Non diabetic animals	OGTT animals
1	Normal control(NC)(Vehicle only)	Normal control(NC)(Vehicle only)	Normal control(NC)+Glucose(2g/kg)
2	Diabetic control (DC)		
3	Aqueous extract 500mg(AEFS)	Aqueous extract 500mg(AEFS)	Aqueous extract 500mg(AEFS)+ Glucose(2g/kg)
4	Methanolic extract 500mg(MEFS)	Methanolic extract 500mg(MEFS)	Methanolic extract500mg(MEFS)+ Glucose(2g/kg)
5	Ethylacetate extract 500mg(EAFS)	Ethylacetate extract 500mg(EAFS)	Ethylacetate extract500mg(EAFS)+ Glucose(2g/kg)
6	Petroleum ether extract 500mg(PEFS)	Petroleum ether extract 500mg (PEFS)	Petroleum ether extract 500mg(PEFS) +Glucose(2g/kg)
7	Glibenclamide 600µg/kg(GLB)	Glibenclamide 600µg/kg(GLB)	Glibenclamide 600µg/kg(GLB)

AEFS:Aqueous extract of F. sarmentosa
MEFS:Methanolic extract of F. sarmentosa EAFS:Ethyl acetate extract of F. sarmentosa
PEFS:PetroleumetherextractofF.sarmentoa

Glibenclamide Preparation :
Pure Glibenclamide (Sun Pharmaceuticals) was given each day by mouth in a 600 µg/kg dose to the diabetic standard control group.

Blood Glucose Measurement :
Sampling was done from the tail vein after the animal had not eaten for 16 hours. Two drops from each drop were tested with a Glucometer [28].

Body Weight Measurement
The scale from ORION Engineering was used to record the body weight of animals on the day of the STZ shot and on Days 1, 4 and 9 (ORION Engineering).

Oral Glucose Tolerance Test (OGTT):
Group I acted as the control, receiving Tween 80; within Group II to XIII, rats fasted and received plant extracts at 500 mg/kg; Group XIV was given 600 µg/kg of Glibenclamide [29]. After half an hour, everyone in the study was given 2 g/kg of glucose. At 0, 30, 60 and 90 minutes following the glucose challenge, blood was taken and looked [30].

Statistical Analysis:
Results were express as mean ± SEM. Statistical analysis was carried out by using one way analysis of the variance followed by Neuman keuls test for comparison between groups. $P<0.05$ was considered as significant.

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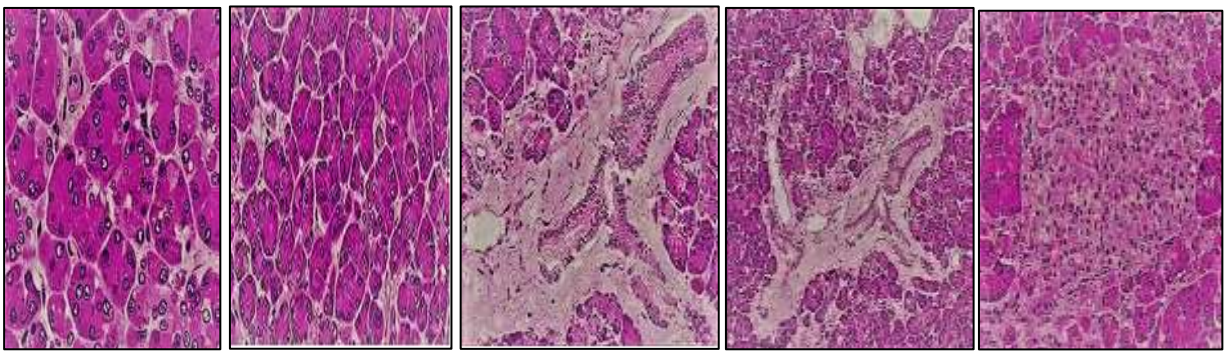

Fig.1 Healthy pancreas

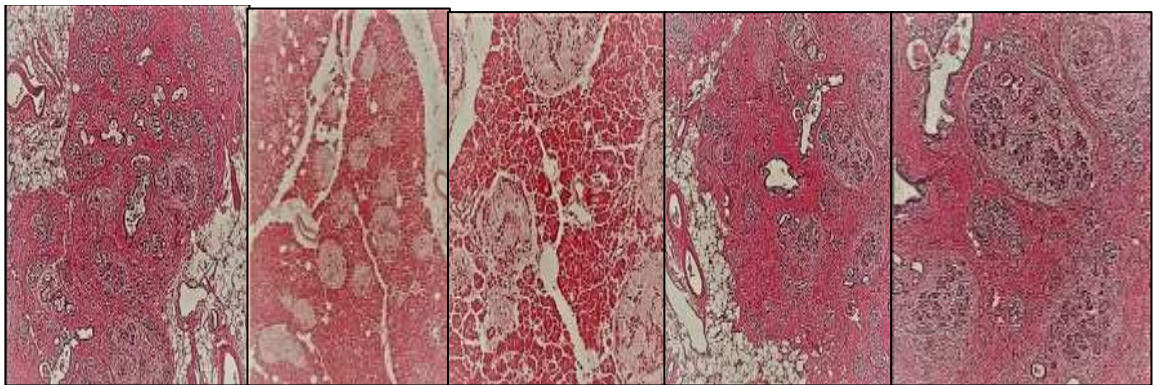

Fig.2 Pancreas after the effects of streptozotocin

RESULT

In the present work, 3 plants were selected on basis of the literature survey & traditional uses from the local area of Chamoli (Garhwal) to screen anti diabetic potential. It was observed that the all plants were extensively used in treatment of different of diseases.

Histopathological studies (Fig.1 & 2) :

The tissues of pancreas received from all of the experimental groups were washed right now with saline and then fixed in 10% buffered impartial formalin answer for 24 hrs. The organs have been dehydrated with a graded collection of ethanol and embedded in paraffin wax [31]. Sections of 5µm had been lessen the use of a microtome (Leica RM2255 Rotary Microtome, United States of America), mounted on glass slides, stained with hematoxylin and eosin (HE) and photographed by means of the use of microscope (Carl Zeiss, united states of america). The variety and size of islets of Langerhans in pancreas had been measured in 10 low electricity subject [32].

Histology of Pancreas (Fig. 2) :

In our study, we chose Ficus sarmentosa (FS) and two other medicinal plants through ethnobotanical data and prior use in Chamoli (Garhwal) to study their antidiabetic effects. The pancreas tissues from STZ-induced diabetic rats were studied using histology chemicals after a treatment period of 9 days(H&E staining, 400×). On H&E slides, normal animals had fully formed islets of Langerhans, whereas too-high blood glucose in the diabetic control made the islets smaller, with a lot of cellular and sclerotic damage affecting many β-cells within them [33]. Fibrosis Score treated groups showed varying degrees of improvement in histopathology. In CNMC animals given EAFS, the islet tissue increased in both number and size, with no evidence of cell death. In addition, the islet structure was improved in the aqueous extract and restored in part in the petroleum extract, but the methanol extract preserved typical islet structure [34].

Toxicity studies:

Tests for acute toxicity were performed in albino Wistar rats in line with OECD protocols. The dose of the

extract was set from 2000 to 5000 mg/kg for the tests [35]. Maximum dosing did not cause any deaths or poisoning symptoms. Therefore, the amount used in the experiments for all FS extracts was 1/10th of the dose shown to be effective (500 mg/kg body weight).

S.No.	Name of Extract	LD_{50} Cut off mg/kgbody weight	Vehicle+Suspendin gagent
1	Aqueous extract(AEFS)	5000 mg	Tween 80
2	Methanolic extract(MEFS)	5000 mg	Tween 80
3	Ethylacetate extract(EAFS)	5000 mg	Tween 80
4	Petroleum ethe rextract(PEFS)	5000 mg	Tween 80

Table 3: LD_{50}Cut off mg/kgbody weight of various extracts

Antidiabetic activity:
Four different extracts of four different plants were screened for antidiabetic activity in STZ induced diabetic rats. Results of antidiabetic activity of FS are mentioned in Table 4.

S.No.	Blood Glucose level mg/100ml													
	Normal Control		Diabetic Control		Glibenclamide		Ficus sarmentosa Extracts							
							Petroleum ether		Ethyl acetate		Methanol		Aqueous	
	Basal value	9th Day	Basal value	9th Day	Basal value	9th Day	Basal value	9th Day	Basal value	9th Day	Basal value	9th Day	Basal value	9th Day
1	73	80	333	347	316	138	314	386	327	153	316	140	332	151
2	79	78	345	336	339	144	324	370	320	152	327	252	347	178
3	76	79	338	341	342	130	317	310	316	189	340	162	313	147
4	76	81	326	335	323	147	316	363	319	216	326	185	352	163
5	69	78	340	342	333	135	319	359	327	280	329	140	335	150
6	75	79	335	338	341	192	345	340	324	162	320	182	327	163
Mean	74.67± 1.382	79.17± 0.477	336.2± 2.651+++	339.8± 1.81++ +	332.3± 4.349	139.2± 2.52***	334.3± 9.265	320.0± 7.58	347.8± 10.37	220.7± 27.2** *	339.2 ±15.42	208.5± 34.9***	322.5± 4.43	201.8± 22.1***
±SD	3.386	1.169	6.494	4.446	10.65	6.178	22.7	18.59	25.4	66.82	37.77	85.54	10.86	54.3

Table 4: Antidiabetic activity of leaves extracts of Ficussarmentosa.

Blood glucose was measured in the fasting state 3 days after the STZ and again on the 9th day of the treatment. Glucose levels in diabetic controls were greatly increased following STZ ($p<0.001$). Glucose levels fell in some animals, but not in others, after being given FS extracts. Both experimental feeding strategies reduced blood glucose levels more than in diabetic animals [36]. AEFS had the most significant decrease among the methods and MEFS showed only a moderate effect. The normalization of blood glucose was also observed with glibenclamide dose (600 µg/kg).

Body Weight Measurement: The body weights of the control rats decreased compared to others. On the other hand, the body weight of extract-treated groups increased during the 9-day treatment. Animals gained the most weight (132.2±1.81 g) on the AEFS diet, followed by the EAFS diet (126.5±1.08 g) and less on the PEFS diet (110.3±2.37 g). The MEFS program made the smallest amount of improvement [37]. Treatment with glibenclamide allowed rats (150.7±1.43 g) to maintain almost regular body weight gains.

Oral Glucose Tolerance Test (OGTT):
Simvastatin treatment markedly improved the ability of rats to tolerate glucose. Thirty and 90 minutes following glucose administration, no and less hyperglycemia was observed in animals who received AEFS or EAFS. Within 90 minutes, people in AEFS had the highest glucose levels (106.5±2.1 mg/dL), in contrast to those in PEFS, with the lowest (121.7±10.06 mg/dL). A similar effect was observed in glibenclamide treated rats (levels were 105.0±0.57 mg/dL) [38].

S.No.	Blood Glucose Level mg/100ml(Mean±SEM)(Ficus sarmentosa)																	
	Normal Control Glucose (2g/kg)(NC)			Glibenclamide Glucose (2g/kg)(NC)			Petroleum ether			Ethyl acetate			Methanol			Aqueous		
	FBGL	30 min	90 min	FBGL	30 min	90 min	FBGL	30 Min	90 min	FBGL	30 min	90 min	FBGL	30 min	90 min	FBGL	30 min	90 min
1	86	197	129	86	187	110	72	171	113	79	168	104	75	179	106	79	189	121
2	84	186	139	89	168	112	73	171	114	78	169	104	68	179	106	82	210	108
3	89	174	126	75	170	101	72	171	113	77	186	103	73	178	105	85	172	103
4	82	177	145	82	174	98	74	171	113	78	168	104	84	179	106	69	159	110
5	79	176	135	69	179	105	72	171	113	78	170	104	89	180	107	81	147	109
6	80	189	140	74	183	108	72	171	113	79	168	104	92	179	107	86	191	100
Mean	83.33 ± 1.54	183.2± 3.68	135.7 ± 2.917	79.17± 3.15	176.8 ± 3.04	105.7± 2.20**	72.67 ± 2.87	171.0 ± 12.9	113.2± 6.45**	78.33± 2.70	168.0± 6.05	104.3± 2.09**	80.17± 3.91	179.3± 4.95	106.5 ± 5.54**	80.33± 2.49	178.0 ± 9.43	108.5± 2.95**
± SD	3.78	9.02	7.15	7.73	7.47	5.39	7.03	31.75	15.82	6.62	14.83	5.12	9.57	12.13	13.58	6.12	23.12	7.23

Table 5: OGTT test

Saponin	tannins	triterpenes	alkaloids	flavonoids	glycoside
+	+	+	+	+	+

(+) present ;(-) absent

Table 6: The phytochemical constituents of the experimental plant fractions obtained by phytochemical screening tests

DISCUSSION

Three medicinal plants from Chamoli (Garhwal) were selected based on traditional usage. Ficus sarmentosa leaves were authenticated and extracted using petroleum ether, ethyl acetate, methanol, and water [39]. The extracts were evaluated for antidiabetic potential through STZ induced diabetic rat models. Phytochemical studies confirmed the presence of bioactive compounds. Aqueous, methanolic and ethyl acetate extracts of FS showed significant blood glucose lowering effects [40]. Histopathological studies revealed islet regeneration and pancreatic protection. Body weight gain in treated groups indicated reversal of diabetic cachexia. Glucose tolerance improved notably in EAFS and MEFS groups, consistent with standard Glibenclamide treatment [41]. And toxicity tests confirmed safety of extracts up to 5000 mg/kg.

CONCLUSION:

It was seen that Ficus sarmentosa leaf extracts, especially ethyl acetate, methanolic and aqueous, strongly decreased blood sugar and raised body weight among diabetic rats [42]. The evidence confirms older beliefs about Ficus species and offers a reason for why they are traditionally used medicine. The plant demonstrated that it was not toxic and might be able to help with pancreatic tissue regeneration, making it helpful for diabetes mellitus.

ETHICAL APPROVAL

Not applicable.

CONSENT FOR PUBLICATION

Not applicable.

HUMAN AND ANIMAL ETHICAL RIGHT

Not applicable.

CONFLICT OF INTEREST

The authors declared no conflict of interest, and no funding was required to conduct these review data.

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AVAILABILITY OF DATA AND MATERIALS

The data supporting this study's findings will be available in the cited references.

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AUTHOR CONTRIBUTION

All authors have equal contribution in the preparation of manuscript and compilation.

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