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ANTI-DIABETIC AND ANTI-ARTHRITIC POTENTIAL OF GLYCOSMIS PENTAPHYLLA STEM BARK IN FCA INDUCED ARTHRITIS AND STREPTOZOTOCIN INDUCED DIABETIC RATS

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ABSTRACT

The anti-diabetic and anti-arthritic potential of the ethonolic extract of stem bark of *Glycosmis pentaphylla* (Rutaceae), a medicinal plant widely used in the traditional Ayurveda and siddha systems of medicine for the treatment by the streptozotocin induced diabetic model and anti-arthritic activity was evaluated by FCA induced arthritis for separate group of animals. Graded doses of the ethonolic extract of *Glycosmis pentaphylla* were administered to experimental arthriticand diabetic rats (different groups) for 21days.Significant ($p \leq 0.01$) reductions in fasting blood glucose levels and inflammation were observed in the respective diabetic and arthritic animals. Increase in Serum insulin levels was observed in diabetic animals due to pancreatic β cell regeneration. There is a significant improvement of the haematological parameters like RBC count, Hb level and the ESR to a near normal level indicating the significant recovery from the anaemic condition and arthritic progress thus justifying its significant role in arthritic conditions. In this study we are focusing the same plant derivatives of *Glycosmis pentaphylla* was used for reducing the complications of diabetes and arthritis in rats.

KEY WORDS: anti-diabetic activity, streptozotocin, glibenclamide, *Glycosmis pentaphylla*, arthritis.

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INTRODUCTION

Traditional and indigenous system of medicine persists all over the world. A number of plant species still remain to be surveyed systematically for their biologically active chemical compounds. Hence phytochemical studies are needed to isolate useful ingredients from traditional herbal drugs[1].

Arthritis is a painful swelling of joints and it is a common disease affecting large population. Osteoarthritis, rheumatoid arthritis and gout are common types. Osteoarthritis is a degenerative joint disease occurring chiefly in older people usually affecting the larger joints initially and deformity and ankylosis develop in late stage. Gout is associated with increased levels of uric acid and deposition of its crystals in joints leading to their destruction of joints[2].

Diabetes mellitus is a heterogeneous metabolic disorder characterized by altered carbohydrate lipid and protein metabolism caused by insulin deficiency often combined with insulin resistance. Diabetes mellitus is classified in to insulin dependent and non-insulin dependent diabetes. Worldwide survey reported that diabetes affecting nearly 10% of the world population[3].There is some evidence for significantly higher levels of insulin resistance in patients with inflammatory arthritis compared with controls and an association between high CRP (C-reactive protein) concentrations and insulin resistance[4].

New research shows that people with diagnosed diabetes are nearly twice as likely to have arthritis, indicating a diabetes-arthritis connection. There are lot of interconnection between diabetes and arthritis. Diabetes causes musculoskeletal changes that lead to symptoms such as joint pain and stiffness; swelling; nodules under the skin, particularly in the fingers; tight, thickened skin; trigger finger; carpal tunnel syndrome; painful shoulders; and severely affected feet. Type 1 diabetes is an autoimmune disease, as is rheumatoid arthritis. In people who have type 1 diabetes, the body attacks the pancreas, the organ where insulin is made, just as RA attacks the synovial tissue lining the joints. Inflammation is the common culprit for both.

Significant numbers of ayurvedic and herbal medicines are also used for the effectiveness, cost of therapy, easy of use and free from the risk of harming of human handling. So there is an increased in demand to use natural products and ayurvedic medicines for anti-arthritic and anti-diabetic activity[5].WHO (1980) has also recommended the evaluation of plants effective and in condition where we lack safe modern drugs. Thus the demand for herbal products with anti-diabetic potential and less side effects increases because insulin therapy is ineffective when given orally and use of oral hypoglycemic drugs lead to side effects[6].

The use of immunosuppressant and synthetic inhibitor leads to hypersensitivity reaction and liver damage thus making the search for safest herbal drugs for arthritis and gout inevitable[7].So there is a need to develop novel herbal formulations for arthritis and diabetes. In this present study the novel herbal formulations are going to be developed for treatment of diabetes and arthritis.

In Hindu medicines, it has been used traditionally in bilious complaints, cough, worms, jaundice and fever. This medicine has been found clinically useful in amoebiasis, dyspepsia, migraine and irritable bowel syndrome. This drug is proved to be effective in bilious complaints like nausea, vomiting, bitter taste in the mouth, heart burn. Juice of leaves is used in fever, liver complaints and as a vermifuge, while leaves are considered good antidote for eczema and other skin troubles[8].

Glycosmis pentaphylla has also been found to have antioxidant, galactagogue, immune stimulant, larvicidal activity, antipyretic and hepatoprotective activities[9].Infolkmedicine, the bark of *Glycosmis pentaphylla* are used for the treatment of diabetes and gonorrhoea[10].

MATERIALS AND METHODS

The plant was collected from the Alagar kovil region, Madurai District and authenticated by a botanist in Madurai. A voucher specimen (GP/JUL/BOT/02) has been kept in our museum for future reference. The bark of the plant were separated and dried under the in room temperature and the dried barks were subjected to size reduction to a coarse powder by using a dry grinder (Philips India) was passed through sieve No.60.

Animals

Healthy, adult male Wistar rats weighing180-200g were used for study. The animals were housed in large and spaces polypropylene cages, maintained under standard condition (12 h Light/ 12h dark cycle) and fed with standard pellet diet (M/S. Hindustan lever Ltd., Bangalore, India) and water *ad libitum*. The study was approved by institutional animal ethics committee of Ultra College of Pharmacy, Madurai. All the animals experimental procedure were carried out as per CPCSEA guideline (CPCSEA No.890/ac/05/CPCSEA).

Preparation of plant extracts

Glycosmis pentaphylla bark were air dried for 3–5 day and 500 g were extracted with absolute 80% ethanol using Soxlet apparatus for 6 h. The extract was evaporated to dryness under reduced pressure at 60◦c (yield 25.6%, w/w, dry weight basis) and the ethanolic extract (EE) stored at 4◦cuntiluse.

Phytochemical analysis

Thealcoholicextractsobtained weresubjectedtopreliminaryphytochemicalscreening[11]to identify the chemical constituents.The methods of analysis employed were those described[12].

Acute toxicity studies

Healthy Wistar rats of either sex were used starved overnight were orally fed with the ethanolic extract in increasing dose levels of 500, 1000, 2000and4000, 5000mg/kgbody weight. The animals were observed continuously for 2 h under the following profiles:

(i) Behavioural profile: Alertness, restlessness, irritability and fearfulness
(ii) Neurological profile: Spontaneous activity, reactivity, touch response, pain response and gait
(iii) Autonomic profile: Defecation and urination. After a period of 24 and 72h animals were observed for any lethality or death.

Anti-diabetic activity in rats

Diabetes was induced by single intraperitoneal injection of freshly prepared streptozotocin (50mg/Kg, Sigma Chemical company St. Louis MO, USA) dissolved in 0.1M citrate buffer (pH4.5) after over-night fasting of 12h.The diabetes was assessed by determining the blood glucose concentration after 48h of streptozotocin injection. The rats with blood glucose level above 200 mg/dL were selected for the experimental studies. To prevent the hypoglycaemia which occurred during the first 24 h following the STZ administration, 5% glucose solution was orally given to the diabetic rats. In all experiments, rats were fasted for 16 h prior to STZ injection. Only rats found with permanent diabetic were used for the antidiabetic study.

Intheexperiment[13-15] a total number of 30 rats (24 diabetic rats, 6 normal rats) was used. The rats were divided into 4 groups of six each.

Group I : Control group (Vehicle treated)
Group II : Diabetic control (streptozotocin 50mg/kg b.w i.p)
Group III : Diabetic rats receiving EE of *Glycosmis pentaphylla* (400 mg/kg bw orally*)*
Group IV : Diabetic rats receiving EE of *Glycosmis pentaphylla* (800 mg/kg bw orally*)*
Group V : Diabetic rats receiving Glibenclamide (0.25mg/kgb.worally)

Standard drug and extract were prepared in 0.5% Carboxy methyl cellulose Suspension as a vehicle and administered orally, Treatment of experimental animals with EE of *Glycosmis pentaphylla* and reference drug were initiated 2 days post streptozotocin

injection and was carried out once daily, by gavage, for 14 days. Food and water were made freely available.

The blood samples were drawn on 0th, 7th, 14th and 21st day from the retro orbital venous plexus of rats under ether anesthesia using a glass capillary tube after a fast of 12 h and the blood was centrifuged (2,500rpm/10min) to getserum. The serum was used for biochemical estimation of fasting blood glucose level[16-18].The Blood glucose level was determined by using glucometer with blood glucose test strips (CONTOUR^{TM}TS).

Anti- arthritic activity in rats

Arthritis was induced by Frenaud's complete adjuvant (FCA) (Difco labs, USA) and this method was described by Newbould. Adjuvant arthritis was induced by subcutaneous injection of FCA (0.1ml) into sub plantar tissue of the right hind paw of each rat.

The animals were divided as follows,

Group 1: Vehicle control (0.5ml 1% w/v Tween 80)

Group 2: Arthritis control

Group 3: Indomethacin 10mg/kg

Group 4: EE of *Glycosmis pentaphylla* 400 mg/kg

Group 5: EE of *Glycosmis pentaphylla* 800 mg/kg

The test group consisted of FCA injected rats challenged with the respective doses of the test drugs administered orally 24h before FCA injection while, the vehicle control rats were injected with 0.1ml of liquid paraffin (incomplete freund's adjuvant) only. The drug treatment was continued daily in the same time after the challenge for 20 more days. The swelling in the injected and contra lateral hind paw are monitored daily using mercury displacement plethysmometer. Increase in the extent of erythema and edema of the tissues shows the severity of the inflammation. The difference between the experimental groups and arthritis control group were analysed. The changes in body weight were recorded daily[19].

RESULTS AND DISCUSSION

Phytochemical Analysis:

Phytochemical screening of both the plant extracts revealed that the presence of flavonoids, alkaloids, glycoside, tannins, saponins and phytosterols.

Acute Toxicity Study

Experiments were carried out on normal healthy rats. The behaviour of the treated rats appeared normal. No toxic effect was seen even with the dose of4 g/kg b.w. and there were no lethality in any of the group. Body weight was normal. Therefore, the cut off dose for effective dose (ED_{50}) was taken as 400mg/kg b.w.which is the 1/10th of LD_{50}.

The effect of ethanolic extract of *Glycosmis pentaphylla* on biochemical parameter in induced diabetes in rats

Groups	Treatment	Total cholesterol	HDL Levels	Triglyceride levels	LDL levels
Group-I	Normal control	73.14 ± 1.42	30.06 ± 0.64	69.13 ± 0.81	35.79 ± 1.19
Group-II	Diabetic control	138.04 ± 0.78***	16.18 ± 0.36***	170.07 ± 1.09***	129.64 ± 0.78***
Group-III	Diabetic + EE(400mg/Kg)	87.90 ± 0.52&&&	24.19 ± 0.43&&&	80.11 ± 0.56&&&	46.52 ± 0.58&&&
Group-IV	Diabetic + EE(800mg/Kg)	84.60 ± 1.16&&&	24.35 ± 0.34&&&	77.12 ± 1.02&&&	44.00 ± 0.94&&&
Group-V	Glybenclamide (0.25mg/Kg)	85.31 ± 0.83$$$	24.17 ± 0.43$$$	79.05 ± 0.60$$$	47.45 ± 1.09$$$

Values are mean ± SEM (N=6). ***P<0.001 as compare to normal control; &&&P<0.001 as compare to Diabetic control, $$$P<0.001 as compare to Diabetic control. One way ANOVA followed by Dunnett's multiple comparison tests.

The effect of ethanolic extract of *Glycosmis pentaphylla* on biochemical parameters in streptozotocin induced diabetes in rats

Groups	Treatment	SGOT	SGPT
Group-I	Normal control	116.33 ± 2.98	88.18 ± 1.07
Group-II	Diabetic control	150.66 ± 1.40***	145.00 ± 2.12***
Group-III	Diabetic + EE(400mg/Kg)	138.16 ± 1.74$^{\&\&\&}$	126.66 ± 1.90$^{\&\&\&}$
Group-IV	Diabetic + EE(800mg/Kg)	131.00 ± 2.73$^{\&\&\&}$	110.83 ± 1.68$^{\&\&\&}$
Group-V	Glybenclamide(0.25mg/Kg)	122.16 ± 2.27$^{\$\$\$}$	99.33 ± 2.21$^{\$\$\$}$

Values are mean ± SEM (N=6). ***P<0.001 as compare to normal control; $^{\&\&\&}$P<0.001 as compare to Diabetic control, $^{\$\$\$}$P<0.001 as compare to Diabetic control. One way ANOVA followed by Dunnett's multiple comparison tests.

The effect of ethanolic extract of Glycosmis pentaphylla on blood glucose levels in streptozotocin induced diabetes in rats.

Overnight fasted rats were divided into five groups of six rats each. Group I, II and V were administered distilled water (control), diabetic untreated control) and standard drug (Glybenclamide0.25mg/kg) by oral route. A dose400 mg/kg and 800 mg/kg of EE of *Glycosmis pentaphylla* were suspended in drug vehicle and administered to group III and group IV orally. The drug vehicle, standard drug and test substance were administered once daily, per orally for the period of 21days.Allthe drug administration procedure was carried out between 8:00-9:30 am of the day. The blood glucose levels were estimated on 0 (pre- study) and 7, 14, 21 day of the study. The rats were restrained in rat restrainer and blood samples were collected from the tail vein by making a small incision on the tail tip and 0.5-1.0 ml of the blood was collected for estimation of blood glucose.

Groups	Treatment	Blood glucose levels (mg/dl) Mean ± SEM				
		1st Day	7th Day	14th Day	21st Day	28th Day
Group-I	Normal control	88.50 ± 3.06	84.84 ±2.00	91.83 ±3.59	88.83 ± 3.13	90.33 ± 2.60
Group-II	Diabetic control	196.16 ± 3.47***	235.66 ±3.38***	295.33 ±7.61***	315.50±8.84***	324.00 ±9.98***
Group-III	Diabetic + EE (400mg/Kg)	192.83 ± 6.87$^{\&\&\&}$	184.50 ±6.85$^{\&\&\&}$	170.16 ±5.31$^{\&\&\&}$	161.50±4.96$^{\&\&\&}$	150.16±2.96$^{\&\&\&}$
Group-IV	Diabetic + EE (800mg/Kg)	195.00 ± 6.24$^{\&\&\&}$	180.66 ±7.41$^{\&\&\&}$	166.50 ±6.54$^{\&\&\&}$	147.33±4.65$^{\&\&\&}$	134.00±3.66$^{\&\&\&}$
Group-V	Glybenclamide (0.25mg/Kg)	190.00 ± 7.42$^{\$\$\$}$	166.50 ± 3.01$^{\$\$\$}$	143.50 ± 7.76$^{\$\$\$}$	120.16 ± 3.78$^{\$\$\$}$	118.50 ± 4.40$^{\$\$\$}$

Values are mean ± SEM (N=6). ***P<0.001 as compare to normal control; $^{\&\&\&}$P<0.001 as compare to Diabetic control, $^{\$\$\$}$P<0.001 as compare to Diabetic control. One way ANOVA followed by Dunnett's multiple comparison tests.

Changes of serum insulin, and glycosylated hemoglobin in normal and streptozotocin induced diabetic rats.

The EE of *Glycosmis pentaphylla* showed significant improvement on serum insulin, and glycosylated hemoglobinin STZ-induced chronic diabetic rat model. Rats were treated with 400 mg/kg b.w and 800 mg/kg b.w of *Glycosmis pentaphylla* for21 day. At the end of the treatment, the animals when compared with diabetic control, showed significant ($p<0.01$) difference in serum insulin level and glycosylated haemoglobin level.

Groups	Treatment	Glucose Concentration(mg/dl)	
		Seruminsulin (ng/ml)	Glycosylated Haemoglobin(%)
Group-I	Normal control	0.26±0.21	3.70±0.09
Group-II	Diabetic control	0.19±0.01***	6.84±0.28***
Group-III	Diabetic + EE(400mg/Kg)	0.28±0.00&&&	3.26±0.42&&&
Group-IV	Diabetic + EE(800mg/Kg)	0.31±0.00&&&	3.48±0.04&&&
Group-V	Glybenclamide(0.25mg/Kg)	0.32±0.02$$$	3.72± 0.18$$$

Values are mean ± SEM (N=6). ***P<0.001 as compare to normal control; &&&P<0.001 as compare to Diabetic control, $$$P<0.001 as compare to Diabetic control. One way ANOVA followed by Dunnett's multiple comparison tests.

The effect of EE of Glycosmis pentaphylla on body weight after streptozotocin induced diabetes in rats.

There was a significant body weight loss in the diabetic rats (Diabetic control) during 21 days, vehicle control animals were found to be stable in their body weight whereas animals treated with EEatthedosesof400mg/kg and 800 mg/kg p.o. showed the significant increase in weight on 14th day onwards, indicatingthat 400mg/kg and 800 mg/kg of EE of plant *Glycosmis pentaphylla* had beneficial effects in preventing loss of body weight of diabetic rats due to increases glucose metabolism.

Groups	Treatment	Average body weight (gm) Mean ± SEM			
		1st Day	7th Day	14th Day	21st Day
Group- I	Normal control	172.33 ± 3.75	173.66 ± 3.98	180.16 ± 3.71	182.00 ± 3.16
Group-II	Diabetic control	174.16 ± 1.56***	166.66 ± 1.94***	151.00 ± 2.00***	130.16 ± 3.28***
Group-III	Diabetic + EE (400mg/Kg)	166.66 ± 3.68&&&	168.66 ± 3.57&&&	173.33 ± 3.53&&&	173.83 ± 3.32&&&
Group-IV	Diabetic + EE (800mg/Kg)	164.83 ± 2.32&&&	167.66 ± 3.57&&&	175.50 ± 1.68&&&	176.16 ± 2.36&&&
Group-V	Glybenclamide (0.25mg/Kg)	166.83± 4.32$$$	170.16 ± 2.96$$$	176.00 ± 2.62$$$	178.83 ± 1.76$$$

Values are mean ± SEM (N=6). ***P<0.001 as compare to normal control; &&&P<0.001 as compare to Diabetic control, $$$P<0.001 as compare to Diabetic control. One way ANOVA followed by Dunnett's multiple comparison tests.

Effect of EE of Glycosmis pentaphylla on FCA induced arthritis in rats

Paw swelling is one of the major factors in assessing the degree of inflammation and curative efficacy of drugs. It occurs through cell mediated-autoimmunity by structural mimicry between mycobacteria and cartilage proteoglycans in rats[20].In the present study, rats were selected to induce arthritis because rats develop a chronic swelling in multiple joints with

influence of inflammatory cells, erosion of joint cartilage and bone destruction[21].

There are also reports on the flavonoidas a potent anti-inflammatory agent; flavonoid may exert its anti-inflammatory activity by inhibiting the 5- lipooxgenase pathway, which together with the COX-2 pathway, is very important in producing and maintaining inflammation[22].

The administration of EE of *Glycosmis pentaphylla* significantly protected against joint swelling in arthritis induced paw when compared with arthritis control group. There was a reduction in paw volume was observed after treating with 400mg/kg however the effect of 800mg/kg treatment was found to be more significant ($p<0.01$).

Treatment	Swelling volume (ml) ± SEM on injected paw										
	Post insult time of assay in days										
	1	3	5	7	9	11	13	15	17	19	21
Normal/ control	0.123 ± 0.0006	0.105 ± 0.0003	0.105 ± 0.0003	0.105 ± 0.0003	0.105 ± 0.0003	0.105 ± 0.0003	0.105 ± 0.0003	0.105 ± 0.0003	0.105 ± 0.0003	0.108 ± 0.0003	0.105 ± 0.0003
Arthritis	0.76±0.008	0.87±0.006	1.05 ±0.006	1.18 ±0.005	0.93± 0.003	0.85±0.006	0.85 ±0.005	0.85 ±0.003	0.86 ±0.006	0.87 ±0.003	0.92 ±0.006
Indomethacin 10mg/kg	0.57± 0.011**	0.68± 0.005**	0.76± 0.01**	0.73± 0.005 **	0.75± 0.017 **	0.75± 0.01**	0.62± 0.02**	0.68± 0.012 **	0.56± 0.008 **	0.56± 0.006 **	0.52± 0.005 **
Arthritic + EE (400mg/Kg)	0.76±0.024	0.86±0.014	1.03 ±0.012	1.16 ±0.003	0.92±0.003	0.84±0.003	0.84±0.003	0.85±0.003	0.86 ±0.005	0.87±0.003	0.92±0.005
Arthritic + EE (800mg/Kg)	0.62±0.011 **	0.76± 0.005**	0.81± 0.01 **	0.78 ±0.00 **	0.76± 0.01 **	0.72± 0.012 **	0.64 ±0.006 **	0.73 ± 0.005**	0.58 ± 0.003 **	0.58±0.003**	0.56 ±0.0 **

Values are expressed as Mean ±SEM, n=6 rats in each group. **P<0.001, significant compared to arthritic control.

Biochemical changes in EE of *Glycosmis pentaphylla* on FCA induced arthritis in rats.

Treatment with EE of *Glycosmis pentaphylla* showed significant ($p<0.05$) increased in body weight as that of vehicle control group. Biochemical parameters include SGOT, SGPT, and Total proteins were highly inhibited while administration of *Glycosmis pentaphylla* and indomethacin treated group.

Treatment	SGOT (U/L)	SGPT (U/L)	Serum copper (µg/dL)	Total protein (U/L)
Normal/control	105.4 ±0.26	55.56 ±0.895	105.76 ±1.910	7.91 ±0.021
Arthritis control	236.56 ±1.009***	156.16 ±0.409***	188.46 ±7.391***	11.33 ±0.033***
Indomethacin 10mg/kg	127.76 ±0881$^{\&\&\&}$	90.86 ±0.218$^{\&\&\&}$	121.3 ±1.060$^{\&\&\&}$	8.6 ±0.05$^{\&\&\&}$
Arthritic + EE (400mg/Kg)	230.6 ±0.6557$^{\$\$\$}$	153.6 ±0.251$^{\$\$\$}$	181.33 ±0.3528$^{\$\$\$}$	11.13 ±0.0881$^{\$\$\$}$
Arthritic + EE (800mg/Kg)	146.53 ±0.731$^{\$\$\$}$	111.83 ±1.185$^{\$\$\$}$	133.56 ±0.8413$^{\$\$\$}$	9.9 ±0.057$^{\$\$\$}$

Values are mean ± SEM (N=6). ***P<0.001 as compare to normal control; $^{\&\&\&}$P<0.001 as compare to arthritic control, $^{\$\$\$}$P<0.001 as compare to arthritic control. One way ANOVA followed by Dunnett's multiple comparison tests.

Haematological changes in EE of Glycosmis pentaphylla on FCA induced arthritis in rats

Arthritic rats exhibited a reduced RBC count, reduced Hb level and an increased ESR and EE of *Glycosmis pentaphylla* treated group improved the RBC count, Hb level and the ESR.

Treatment	WBCcells/cu.mm	RBCcells/cu.mm	ESR mm/hr	Hbgm/dl
Normal/control	7.35±0.005	4.82±0.05	3.30±0.005	12.66±0.08
Arthritis control	7.86±0.005***	3.74±0.109***	7.06±0.003***	8.92±0.00***
Indomethacin 10mg/kg	7.03±0.01$^{\&\&\&}$	4.65±0.03$^{\&\&\&}$	4.07±0.03$^{\&\&\&}$	11.72±0.05$^{\&\&\&}$
Arthritic + EE (400mg/Kg)	7.85±0.003$^{\$\$\$}$	3.76±0.07$^{\$\$\$}$	7.02±0.03$^{\$\$\$}$	8.06 ±0.30$^{\$\$\$}$
Arthritic + EE (800mg/Kg)	7.16±0.003$^{\$\$\$}$	4.62±0.01$^{\$\$\$}$	4.58±0.03$^{\$\$\$}$	10.16 ±0.03$^{\$\$\$}$

Values are mean ± SEM (N=6). ***P<0.001 as compare to normal control; $^{\&\&\&}$P<0.001 as compare to arthritic control, $^{\$\$\$}$P<0.001 as compare to arthritic control. One way ANOVA followed by Dunnett's multiple comparison tests.

CONCLUSION

The anti-diabetic activity of *Glycosmis pentaphylla* was found to be non-toxic and well tolerated after following chronic oral administration. It is concluded that *Glycosmisp entaphylla* is safe and strong anti-diabetic activity and efficacy of both doses (400 mg/kg and 800 mg/kg) of extracts was almost comparable to that of glybenclamide. The results presently discussed concluded the *Glycosmis pentaphylla* exert potent anti-arthritic activity by significantly altering the pathogenesis during arthritic without exerting any side effect in FCA induced arthritis in rats. The final conclusion was the same plant derivatives of *Glycosmis pentaphylla* were used for reducing the complications of diabetes and arthritis in rats.

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