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## COMPARATIVE STUDY OF HYPOGLYCEMIC EFFECTS AND ANTIOXIDANT POTENTIAL OF POLYHERBAL FORMULATION IN ALLOXAN INDUCED DIABETIC RATS AN ALTERNATIVE THERAPEUTIC AGENT FOR DIABETES MANAGEMENT

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### Keywords:

Antidiabetic, Polyherbal,  
Alloxan, Antioxidant, Metformin

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**ABSTRACT:** Objective: Comparative screening of Polyherbal preparations for anti-diabetic and antioxidant activity in rats. Materials and Methods: The blood glucose lowering activity of the Polyherbal preparation 1 and 2 was studied in normal rats and alloxan-induced diabetic rats after oral administration at doses of 1.0 ml/kg body wt. Blood samples were collected from the tail vein method on 1, 7, 15, and 23<sup>rd</sup> day. Biochemical parameters like SGOT, SGPT, Liver Glycogen, Urea, Creatinine, LDL, Cholesterol etc were evaluated. Effect was also observed on antioxidant activity and learning and memory dysfunction in diabetes. The data was compared statistically using the one-way ANOVA method followed by the Dunnett test. Results: The Polyherbal preparation 1 and 2 produced significant ( $P < 0.05, 0.01$ ) reduction in the blood glucose level and other biochemical parameters in diabetic rats after 23 days of study compared with that of control and Metformin. They also have significant antioxidant activity effective in diabetic neuropathy and learning and memory dysfunction. Conclusion: The Polyherbal preparation 1 and 2 showed antidiabetic in diabetic rats. This preparation can be used as an alternative to anti-diabetic preparation. However, it requires further extensive molecular level studies for identifying mechanism of actions.

**INTRODUCTION:** Diabetes Mellitus consists of a group of disorders characterized by hyperglycemia, altered metabolism of lipids, carbohydrates, and proteins and an increased risk of complications from vascular disease.

The metabolic consequences of prolonged hyperglycemia and dyslipidemia, including accelerated atherosclerosis, chronic kidney disease, and blindness, pose an enormous burden on patients with DM and on society. Improvements in our understanding of the pathogenesis of diabetes and its complications and in the prevention and therapy of diabetes are critical to meeting this challenge <sup>1</sup>. Herbal formulations have been used by the majority of Indians since ancient times.

In recent years, there has been an increased inclination towards the herbal formulations due to

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the trend towards the natural sources and a healthy life style. Moreover, the complexity, side effects and costly treatment associated with the allopathic medicines have caused both the health care practitioners and the majority of world populations to turn towards alternative therapies, more likely towards the herbal medicines <sup>2</sup>.

Most of the hypoglycemic agents and hypolipidemics used in allopathic practice to treat diabetes mellitus and hyperlipidemia are reported to have side effects in long term use <sup>3</sup>. Hence, there is the need to search for effective and safe drugs for these ailments. Neuropathy is the major reason for morbidity and mortality among diabetic patients. Oxidative stress has been suggested as a major contributor to the diabetic neuropathy.

Increased production of reactive oxygen species and decreased antioxidant defense in diabetic neuropathy has been reported. Metabolic diseases such as diabetes and obesity have been associated with increased vulnerability to stress <sup>4</sup> and cognitive dysfunction <sup>5</sup>. Diabetes mellitus can lead to functional and structural deficits in both the peripheral and central nervous system. The pathogenesis of these deficits is multifactor and may involve microvascular dysfunction and oxidative stress <sup>6</sup>.

#### Drug:

##### Polyherbal:

**Ingredients:** *Syzygium cumini*, *Inula racemosa*, *Ricinus Communis*, *Boerhavia diffusa*, *Zingiber Officinale*, *Acorus calamus*, *Askand*, *Asparagus racemosus*, *Symplocos racemosa*, *Woodfordia fruticosa* etc.

#### Drug:

##### Polyherbal:

**Ingredients:** *Syzygium cumini*, *Momordica charantia*, *Punica Granatum*, *Gymnema sylvestre*, *Withania somnifera*, *Asphaltum*, *Chlorophytum Borivilianum*, *Allium sativum*, *Piper longum*, *Emblie Myrobalan*, *Aloe barbadensis* etc.

### MATERIALS AND METHODS:

#### Collection of Drugs:

The polyherbal preparations 1 and 2 were purchased from the local market.

### Dose and route of administration:

List of chemicals along with their doses and route of administration

S. no.	Chemical	Dose	Route
1.	Alloxan	150 mg/kg	Intraperitoneal
2.	Glucose	5%	Oral
3.	Metformin	120 mg/kg	Oral
4.	Polyherbal 1	1ml/kg	Oral
5.	Polyherbal 2	1ml/kg	Oral

### Volume of administration:

The volume of administration (Oral and i.p.) was calculated based on the route of administration and body weight of animals and was kept constant.

### Storage condition:

All the drugs and solutions were prepared freshly and used on the day of dosing. The solutions were stored, if required, in airtight amber coloured vials in the refrigerator. Swiss albino rats weighing between (125-200gm) were used. They were maintained at temp of  $25 \pm 2^\circ\text{C}$  and relative humidity of 45 to 55% and under standard environmental conditions (12 h. light /12 h. dark cycles). The animals had free access to food and water. Animals were obtained from Aurangabad, Maharashtra, India. All the experiments were carried out between 9 to 18 hrs. The experimental protocol was approved by Institutional Animal Ethics Committee (IAEC) of Y. B. Chavan College of Pharmacy, Dr Rafiq Zakaria Campus, Aurangabad. (Approval number-CPCSEA/IEAC/P'col-18/2011-12/42). The animals were randomly divided into five groups, each group contained six animals.

### Daily acclimatization of animals:

The animals were shifted from animal house to the laboratory one hour prior to the experiment. The respective apparatus were cleaned with ethanol and damp cloth wherever necessary to avoid possible bias due to odour left by the previous used animal.

### Induction of Experimental diabetes:

Overnight fasted experimental rats from groups 2, 3, 4, 5 were injected with Alloxan (Sigma, USA) at a dose of 150 mg/kg body weight <sup>7</sup>. The chemical was injected intraperitoneally (i.p) within 10 min after dissolving in distilled water. The rats in group 1 were injected with distilled water as a vehicle

control. The animals were allowed to drink 5% glucose solution overnight to overcome the drug induced hypoglycemia. Fasting blood glucose (FBG) was estimated at the time of induction of diabetes and postprandial glucose (PPG) was checked regularly until stable hyperglycemia was achieved. After a week time for the development of diabetes, the rats with moderate diabetes having glycosuria and hyperglycemia (blood glucose levels of 250 mg/dl) were included in the study as stable hyperglycemic animals. Once the stable hyperglycemia was achieved, the rats belonging to group 5 were treated with an oral dose of

metformin (120 mg/kg bw), Group 4 with Polyherbal 2 (1ml/kg), Group 3 with Polyherbal 1(1ml/kg), once every day for 15 consecutive days while groups 1 and 2 rats received only Distilled water (as vehicle control).

## RESULTS:

As shown in **Tables 2, 3, 4** and **5** there was significant reduction in blood glucose, other biochemical parameters and also diabetic neuropathy and learning and memory dysfunction. As shown **Fig. 1-7**.

**TABLE: 1 GROUPS AND TREATMENT**

Groups	Treatment	Dose
1	Normal control	Distilled water
2	Diabetic control	Distilled water
3	Polyherbal 1	1 ml/kg
4	Polyherbal 2	1ml/kg
5	Metformin (Standard)	120 mg/kg

After 15 days of treatment with Polyherbal 1 and 2 all the tests for diabetic neuropathy and for learning and memory dysfunction were carried out and the results obtained are given below

## Blood Glucose:

**TABLE 2: EFFECT OF POLYHERBAL 1 AND POLYHERBAL 2 ON FASTING BLOOD GLUCOSE.**

Animal: Rats Alloxan: 150mg/kg, i.p.

Group	Treatment	Fasting blood glucose level (mg/dl)			
		Initial	1 <sup>st</sup> week	2 <sup>nd</sup> week	3 <sup>rd</sup> week
1	Normal Control	127.6±3.6	126.8±3.3	128.8±2.5	129.8±3.4
2	Diabetic control	132.6±5.5	325±15.5	309±8.4	309.6±7.7
3	Diabetic + Polyherbal 1 (1ml/kg)	122.8±2.3*	287±8.5**	155.5±3.4**	139.6±3.7*
4	Diabetic +Polyherbal 2 (1ml/kg)	132.6±5.2*	306.1±3.7**	175.5±3.2**	156.8±5.4**
5	Diabetic + Metformin (120mg/kg)	132.±4.7*	305.5±6.5**	163.8±4.5**	153±3.7*

Results are expressed as Mean ± SEM (n=6). The data was analysed using One-way Analysis of Variance (ANOVA) followed by *Dunnnett's- test*. \*P < 0.5, \*\*P < 0.01 vs Control

## Diabetic Neuropathy Results:

**TABLE:3 EFFECT OF POLYHERBAL 1 AND POLYHERBAL 2 TREATMENT ON NEUROPATHY MODELS**

Group	Treatment	Paw Withdrawal Latency (in Sec)	Tail Flick Withdrawal Latency (in Sec)	Hot Water Immersion Tail withdrawal latency (in sec)	Cold Water Tail Immersion withdrawal latency (in sec)	Rotarod Latency (in sec)
1	Normal Control	12.9±0.48	1.71±0.10	4.3±0.15	8.4±0.20	262.5±15.5
2	Diabetic control	8.05±0.60	1.34±0.03	2.34±0.16	3.7±0.20	44.8±4.4
3	Diabetic+ Polyherbal 1 (1ml/kg)	14.5±0.33**	3.19±0.16*	4.72±0.14**	9.9±0.29*	199.5±21.2**
4	Diabetic+Polyherbal 2 (1ml/kg)	16.6±0.42*	2.70±0.09*	4.29±0.15**	12.1±0.31*	139±9.8*
5	Diabetic+Metformin (120mg/kg)	13.2±0.55**	2.72±0.08*	4.38±0.17**	7.7±0.28**	119±10.4*

Results are expressed as Mean ± SEM (n=6). The data was analysed using One-way Analysis of Variance (ANOVA) followed by *Dunnnett's- test*. \*P < 0.01, \*\*P < 0.05 vs Control.

Learning and memory dysfunction results:

**TABLE: 4 EFFECT OF POLYHERBAL 1 AND POLYHERBAL 2 TREATMENT ON LEARNING AND MEMORY DYSFUNCTION MODELS**

Group	Treatment	Elevated Plus Maze Test		Object Recognition Test		Open Field Test	
		Transfer latency(seconds)		Exploration (Seconds)		Numbers of squares/rearing	
		Central platform	Familiar object	Novel object	Closed arm	Locomotor activity	Rearing
1	Normal Control	5.9±0.21	5.5±0.51	5.9±0.47	20.3±1.5	46.1±3.5	33.5±2.3
2	Diabetic control	13.5±0.90	2.5±0.20	1.7±0.45	50.5±12.9	24.3±3.02	15.5±1.6
3	Diabetic + Polyherbal 1 (1ml/kg)	7.4±0.60**	5.1±0.35**	5.1±0.25**	19.3±2.3**	41.8±2.2**	30.1±4**
4	Diabetic +Polyherbal 2 (1ml/kg)	8.9±0.53*	3.9±0.31**	6.7±0.62**	20.1±1.7**	37.6±2.3**	24±2**
5	Diabetic + Metformin (120mg/kg)	10.9±0.51*	3.8±0.26*	5.2±0.38**	21.8±1.4**	37±3.2**	25.5±2.7**

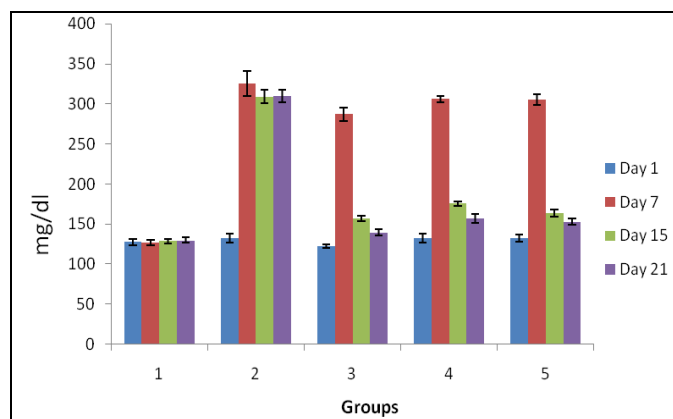
Results are expressed as Mean ± SEM (n=6). The data was analysed using One-way Analysis of Variance (ANOVA) followed by *Dunnnett's- test*. \*P < 0.01\*\*P < 0.05 vs Control.

**TABLE 5: EFFECT OF POLYHERBAL 1 AND POLYHERBAL 2 ON BIOCHEMICAL PARAMETERS.**

Grp	Treatment	CRP (mg/dl)	LDL (mg/dl)	Liver Glycogen(mg/2 gm liver wt)	SGOT (mg/dl)	SGPT (mg/dl)	Triglycerides (mg/dl)	Urea (mg/dl)	Creatinine mg/L
1	Normal Control	0.29±0.02	33.6±1.9	2.1±0.06	58.3±1.8	49±3	92.1±2.4	36.5±1.4	1.05±0.04
2	Diabetic control	1.49±0.09	75.5±4.1	1.49±0.09	169±6.2	155.5±9.09	188.8±11.5	76±3	2.24±0.09
3	Diabetic + Polyherbal 1 (1ml/kg)	0.65±0.06*	39.1±2.1*	2.27±0.07**	85.1±5.5**	64.6±7.5**	96.8±3.9**	41±1.3**	0.93±0.09**
4	Diabetic +Polyherbal 2 (1ml/kg)	0.61±0.04*	26.3±1.4*	2.25±0.11**	106.8±10.7*	57.5±4.5**	98.6±3.9**	45.1±3.3**	0.96±0.08**
5	Diabetic + Metformin (120mg/kg)	0.79±0.05*	32.8±2.7*	2.07±0.06**	114.1±7.1*	64±6.1**	100.3±4.2**	47.8±3**	1.1±0.06**

Results are expressed as Mean ± SEM (n=6). The data was analysed using One-way Analysis of Variance (ANOVA) followed by *Dunnnett's- test*. \*P < 0.01 and \*\*P < 0.05 vs Control.

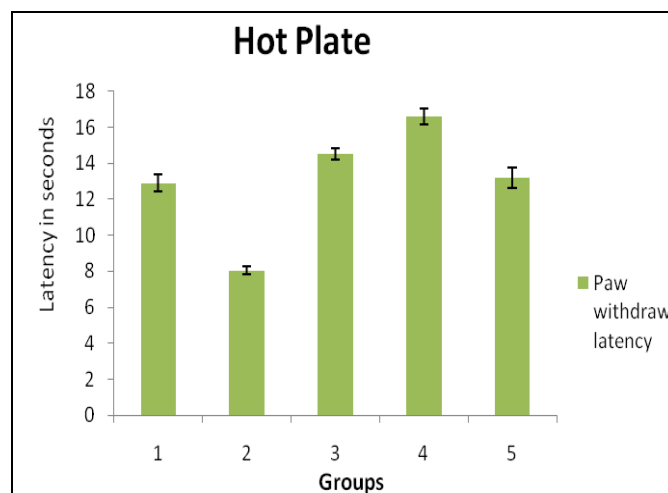
**Effect of Polyherbal 1 and Polyherbal 2 on fasting blood glucose:**



**FIG.1: BLOOD GLUCOSE**

Results are expressed as Mean ± SEM (n=6). The data was analysed using One-way Analysis of Variance (ANOVA) followed by *Dunnnett's- test*. \*P < 0.01 and \*\*P < 0.05 vs Control.

**Effect of Polyherbal 1 and Polyherbal 2 treatment on Neuropathy models:**



**FIG.2 HOT PLATE**

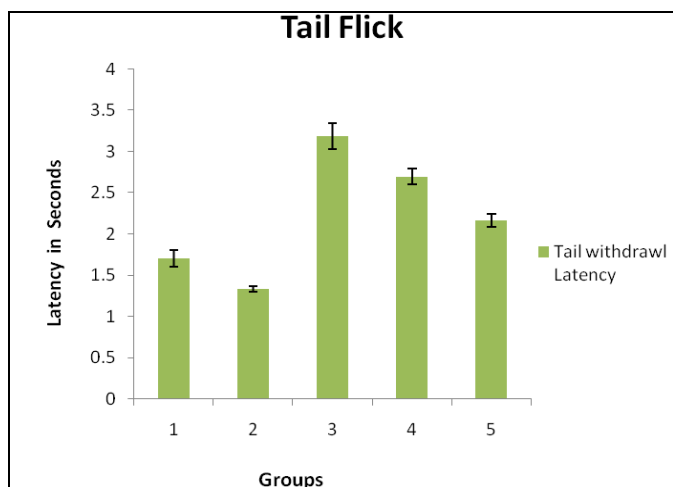


FIG:3 TAIL FLICK

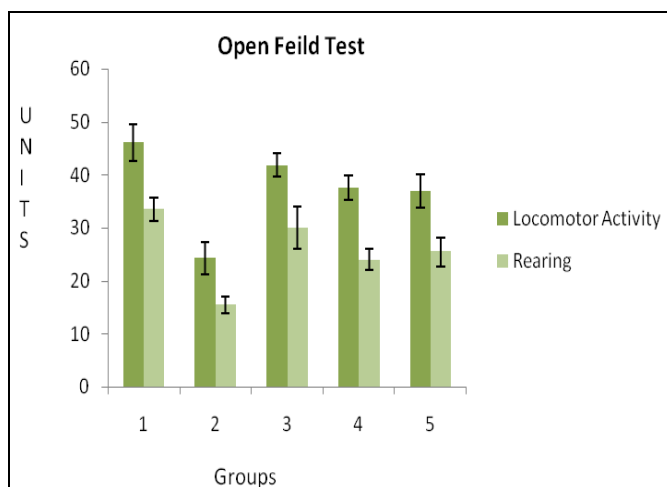


FIG:6 OPEN FIELD TEST

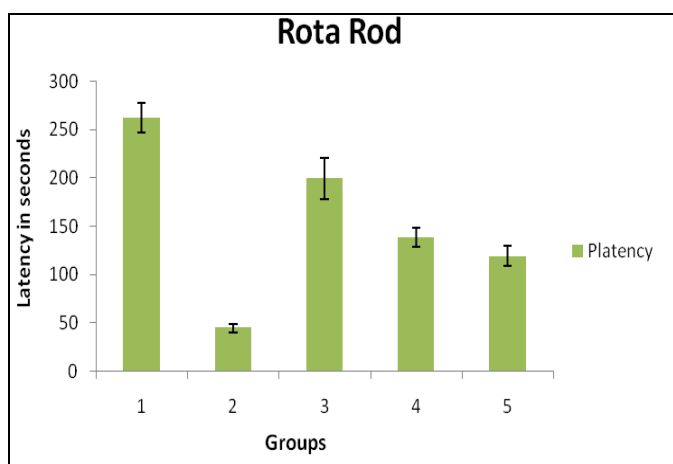


FIG:4 ROTA ROD

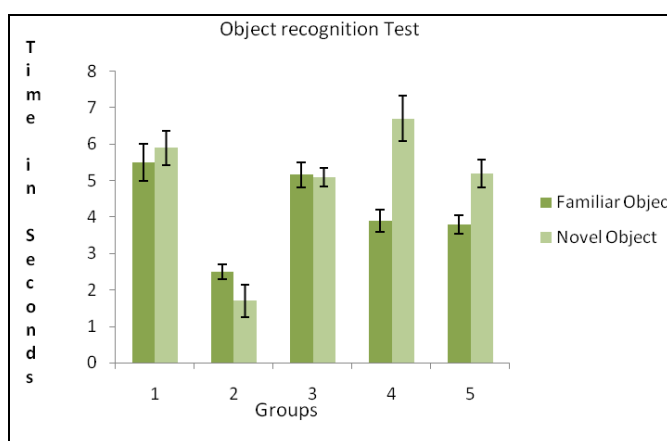


FIG:7: OBJECT RECOGNITION TEST

Results are expressed as Mean  $\pm$  SEM (n=6). The data was analysed using One-way Analysis of Variance (ANOVA) followed by *Dunnett's- test*. \*P < 0.01 and \*\*P < 0.05 vs Control

Results are expressed as Mean  $\pm$  SEM (n=6). The data was analysed using One-way Analysis of Variance (ANOVA) followed by *Dunnett's- test*. \*P < 0.01 and \*\*P < 0.05 vs Control

### Effect of Polyherbal 1 and Polyherbal 2 treatment on Learning and Memory Dysfunction Models:

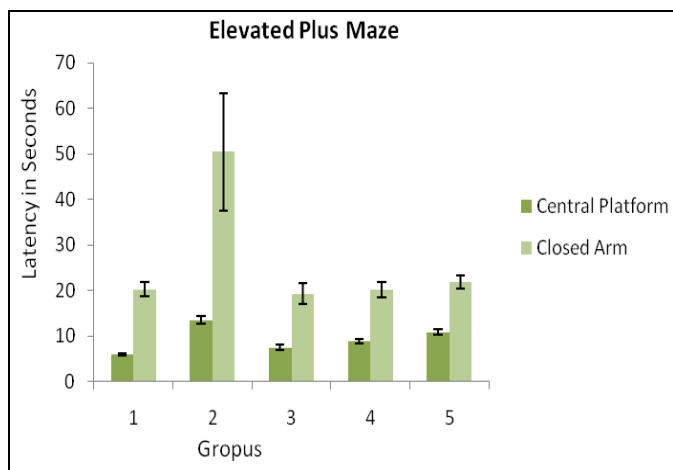


FIG:5: ELEVATED PLUS MAZE

**DISCUSSION:** The concept of efficacy in phytotherapy is based on the mixture of substances contained in the medicinal plants and the polyherbal formulations composed of more than one herbal ingredient have specific time proven therapeutic values<sup>8</sup>. Treatment with Polyherbal formulation 1 and 2 and Metformin lowered elevated blood glucose level, which was high in diabetic control animals. Maximum reduction in the blood glucose level was noted with Polyherbal formulation 1.

Thus Polyherbal formulation 1 proved significant hypoglycemic activity in diabetic rats, which was comparable to the standard drug used i.e. Metformin. Polyherbal formulation 1 and 2 and Metformin significantly decreased the serum lipids level and serum enzyme levels of SGOT and

SGPT. The main ingredient of these Polyherbal preparations is *Syzygium cumini*. In India decoction of kernels of *Eugenia jambolana* is used as a household remedy for diabetes it ameliorates Insulin Resistance and  $\beta$ -Cell Dysfunction via Modulation of PPAR $\gamma$ , Dyslipidemia, Oxidative Stress, and TNF- $\alpha$  in Type 2 Diabetic Rats<sup>9</sup>. Effect on other biochemical parameters like LDL, Urea, Creatinine, Triglycerides and CRP was also beneficial. **Table 5**

Alloxan-induced diabetic model exhibits a profound hyperalgesia and motor in coordination which was evident within 2 weeks of alloxan injection and lasted for at least 4 weeks<sup>10</sup>. Diabetic rats with autonomic neuropathy presented lower scores in cognitive tests of memory than non-diabetic subjects. **(Table 4)**

Neuropathic pain is the most common symptom associated with diabetic neuropathy. Alloxan injected rats had significantly higher blood glucose level, decreased body weight and the nociceptive threshold was significantly lower than non-diabetic rats in hot plate, tail flick, hot and cold water tail immersion, indicating that diabetic animals exhibit thermal hyperalgesia. In Rota rod test motor in coordination was observed in diabetic animals. Treatment with Polyherbal 1 and Polyherbal 2 restored body weight, blood glucose, along with pain threshold and motor in coordination in diabetic rats. Hyperglycemia effects locomotor activity and learning and memory also<sup>11 12</sup>. **(Table 3, 4)**

**PHB 2:** The antioxidant effect may be due to *Punica Granatum*, pomegranate juice exerts significant antioxidant activity in diabetes patients without affecting the blood sugar levels. This helps reduce the oxidative stress caused by free radicals formed as a result of various metabolic processes in the body and also prevents atherosclerosis, or plaque formation in the blood vessels. Pomegranate juice may also improve insulin sensitivity and lower the risks of developing type 2 diabetes in the first place<sup>13 14</sup>. *Emblic Myrobalan* also have strong free radical scavenging activity. It relieves the oxidative stress and improving glucose metabolism in diabetes and stimulates pancreas<sup>15</sup>. *Momordica Charantia* juice acts against free radical mediated

oxidative damage to biomolecules and membranes<sup>16</sup>. Asphaltum having Fulvic acid successfully eradicates free radical damage to pancreatic islet beta cells, a leading cause of diabetes<sup>17 18</sup>. *Inula racemosa* enhances peripheral sensitivity of insulin action<sup>19</sup>. *Inula* has antioxidant properties because greater availability of GSH to the cell leads to higher rate of destruction of deleterious hydrogen peroxide and lipid peroxides by glutathione peroxidase and hence, protection of vital biomolecules, nucleic acids, carbohydrates, proteins and lipids against oxidative injury associated with chemical toxicity and certain diseases<sup>20</sup>.

The hypoglycemic effect of *I racemosa* could be because of increased utilization of Glucose by peripheral tissues without affecting insulin secretion, additionally because of beta blocking activity it might be sensitizing insulin receptor in the periphery. Its cortisol lowering activity along with antiperoxidative and hypoglycemic activity has been reported. *I racemosa* possess large number of sesquiterpene lactones and essential oils responsible for antidiabetic and antioxidant activity<sup>21</sup>. *Ricinus communis* The beneficial effects is possibly due to the flavonoids present in *R. communis*, roots are known to possess free radical scavenging activity. The mechanism of antidiabetic activity may be its protective role in quenching free radicals and thus beneficial in survival of pancreatic beta cells<sup>22</sup>. The *B diffusa* leaves are rich in alkaloids and sterols including ursolic acid, hypoxanthine-9-L-arabinofuranoside, punarnavine 1 and 2, myricyl alcohol, myristic acid and quinolizidine alkaloids.

These compounds may be responsible for the antioxidant and antidiabetic activity of *B. diffusa* leaves, which may be attributed to its protective action on lipid peroxidation and to the enhancing effect on cellular antioxidant defense contributing to the protection against oxidative damage in alloxanized diabetes<sup>23</sup>. These profound effects of *B. diffusa* root extract against oxidative plasmid DNA damage, antioxidant and  $\alpha$ -amylase inhibitory activity explains its extensive use in daily life and possible health benefits<sup>24</sup>. *Zinziber officinalis* of PHB 2 reduces the marked rises in body weight, serum glucose, insulin, total

cholesterol, LDL, triglycerides, free fatty acid, and phospholipids induced by high-fat diet significantly<sup>25</sup>. It alleviates signs of metabolic syndrome, including decrease of blood glucose, total lipid, and an increase in total antioxidant level<sup>26</sup>. It shows better glucose tolerance and enhanced serum insulin concentration in diabetic rats<sup>27</sup>. Furthermore, the major pungent component in ginger, [6]-gingerol significantly decreases fasting blood glucose and improves glucose tolerance in db/db type 2 diabetic mice and lowers plasma triglyceride, total cholesterol, free fatty acid, low-density lipoprotein, and plasma insulin levels<sup>28</sup>. *Acorus calamus* in diabetic rats reduces the activity of AST, ALT and ALP in plasma compared to the diabetic untreated group and consequently alleviates liver damage<sup>29</sup>. It has insulin releasing, insulin sensitizing and alpha glucosidase inhibiting activity<sup>30</sup>. *Asparagus racemosus* shows significant antidiabetic activity, antihyperlipidemic and antioxidant properties in diabetic rats<sup>31</sup>.

Prolonged exposure to high glucose concentrations (hyperglycemia) promotes the development of microvascular complications associated with diabetes mellitus<sup>32</sup>. Such complications affect the kidneys (nephropathy), eyes (retinopathy), heart (cardiomyopathy), nerves (neuropathy) and blood vessels<sup>33</sup>. It is well accepted that, the high oxidative stress in diabetics considerably contributes to the complication of this disease<sup>34</sup>. *Symplocos racemosa* potentiates, the pancreatic secretion of insulin from regenerated beta-cells, or its action to release bound insulin from regenerated beta cells by inhibiting ATP sensitive K<sup>+</sup> channels like glibenclamide. It showed the presence of beta sitosterol which has antioxidant antidiabetic and antilipidemic activity<sup>35</sup>. *Woodfordia fruticosa* again of PHB 2 possess potential antihyperglycemic effect by regulating glucose homeostasis and antioxidant efficacy in diabetic rats<sup>36</sup>.

**PHB 1:** Has *M. charantia* which contains at least one ingredient with selective 11 $\beta$ -HSD1 inhibitory activity<sup>37</sup>. As such, *Momordica charantia* increases the renewal of beta-cells in the pancreas or may permit the recovery of partially destroyed beta-cells<sup>38</sup>, remarkably stimulates glycogen storage by the liver and improves peripheral glucose uptake<sup>39</sup>. *Punica granatum* stimulates the

expression of the PPAR- $\gamma$  gene<sup>40</sup>. *Withania somnifera* and *Aloe vera* are more effective in reducing oxidative damage in brain regions than the supplementation of single plant extract. The combination also lowers the blood glucose level. Memory impairment and motor dysfunction are also improved by the plant extracts supplementation<sup>41</sup>. *Chlorophytum borivilianum* also has significant antidiabetic activity<sup>42</sup>. *Allium sativum* decreases significantly the concentration of serum lipids, blood glucose and activities of serum enzymes like alkaline phosphatase, acid phosphatase and lactate dehydrogenase and liver glucose-6-phosphatase.

It increases significantly liver and intestinal HMG CoA reductase activity and liver hexokinase activity<sup>43</sup>. *Piper nigrum* seeds are similar to insulin in having a hypoglycemic effect, they also check the antioxidant level<sup>44</sup>. *Aloe* decreases oxidative load. The *Aloe barbadensis* also act by either directly scavenging the reactive oxygen metabolites, due to the presence of various antioxidant compounds or by increasing the synthesis of antioxidant molecule<sup>45</sup>.

Open field test observations indicated that the impaired performance of diabetic rats is related to cognitive dysfunction rather than thymotaxic behavior, since the number of locomotor counts and rearing of diabetic rats were decreased to non-diabetic rats. PHB 1 also prevented motor incoordination seen in diabetic neuropathy. PHB 2 is also very effective in preventing motor incoordination. The EPM test is a simple method for the evaluation of learning and memory process. Since the animals are able to remember the configuration of the open and enclosed arms, they escape from the unsafe open arm more rapidly on the second trial.

It is possible to evaluate the fear motivated learning, which underlies the transfer latency procedure in this test. Shortened transfer latency on third day's trial in rats is used as a parameter for retention or consolidation of memory. Transfer latency of Polyherbal treated rats was less comparable to normal rats showing that they are effective in memory dysfunction also. In object recognition test exploration of the animal to the

novel object and familiar object is similar indicating memory impairment in diabetic rats. The current study explored the findings demonstrating that diabetes reduced learning and memory performance, whereas PHB 2 was very effective in showing positive effect in open field test shown by increased exploration of novel object than familiar object.

**CONCLUSION:** The roles of oxidative stress in nerve damage have been studied extensively in experimental diabetes and diabetic patients<sup>46</sup> However, oxidative stress also contributes to the cognitive dysfunction during hyperglycemia. Oxidative damage to the synapses in the rats cerebral cortex and hippocampus is reported to contribute to the deficit of cognitive functions. Therefore, anti-oxidants might be of use in the prevention of the neurodegeneration and cognitive dysfunctions associated with diabetes<sup>47</sup>

Polyherbal 1 and 2 were also effective in Diabetic neuropathy maybe due to antioxidant activity. Therefore, the reversal of hyperalgesia and restoration of cognitive function was observed in diabetic rats. As diabetes is a multifactorial disease leading to several complications, and therefore demands a multiple therapeutic approach<sup>48 49</sup>. Therefore Polyherbals were found to be very effective in Diabetes and Diabetic complications. The formulation Polyherbal 1 was found to be more efficacious as compared to Polyherbal 2. The significant antidiabetic activity of polyherbal formulations may be due to inhibition of free radical generation and subsequent tissue damage induced by alloxan or potentiation of plasma insulin effect by increasing either pancreatic secretion of insulin from existing beta cells or its release from bound form as indicated by significant improvement in glucose and protein level because insulin inhibit gluconeogenesis from protein.

**FUTURE PROSPECTS:** Natural drugs from traditional Indian medicine are gaining popularity because of several advantages such as fewer side-effects, better patient tolerance, relatively less expensive and acceptance due to a long history of use. The more important cause is that natural products, especially herbal medicines provide rational means for the treatment of many diseases

that are obstinate and incurable in other systems of medicine.<sup>50</sup>

**CONFLICT OF INTEREST STATEMENT:** We declare that we have no conflict of interest.

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