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Pharmacological Evaluation of Colocaciaesculanta Leaves on Diabetic Neuropathic pain by using Animal model

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Abstract: *Diabetes is a metabolic disorder characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion and leading to various complications, including diabetic neuropathy (DN), characterized by nerve damage and neuropathic pain.The current studyevaluated the effect of Methanolic Extract ofColocaciaesculanta (MECE) leaves on diabetic neuropathic pain in streptozotocin (STZ)-induced diabetic rats. Diabetes was induced in Male Wistar rats via STZ injection (60 mg/kg).Diabetic neuropathy was confirmed after STZ induction in negative control group assessing thermal hyperalgesia using the tail flick test and motor coordination deficits using therota rod apparatus and Swimming Endurance Test (SET) model. Diabetic rats were then treated orally withMECE at low (150 mg/kg) and high (300 mg/kg) doses, and Metformin (25 mg/kg) as a standard control. The effects of MECEon pain threshold (tail flick latency) and motor coordination (Swimming Endurance Test (SET)and rota rod falling time) were evaluated. Phytochemical screening of (MECE) revealed the presence of alkaloids, Flavonoids, carbohydrates,Steroid, tannins, proteins. The results demonstrated that STZ-induced diabetic rats exhibited significant thermal hyperalgesia and impaired motor coordination compared to normal control rats. Treatment with both low and high doses of MECE significantly improved tail flick latency, Swimming activity and rota rod falling time in diabetic rats compared to theNegative control group. These findings suggest that MECE possesses potential analgesic and neuroprotective effects in the context of diabetic neuropathic pain in rats.*

Keywords: *Colocaciaesculanta*, Diabetic Neuropathic Pain, Streptozotocin, Tail Flick Test, Swimming Endurance Test (SET), Rota Rod Test

I. INTRODUCTION

Diabetes is a metabolic disorder characterized by chronic hyperglycaemia with disturbances ofcarbohydrate, fat and protein metabolism resulting from defects in insulin secretion and leading to various complications, including diabetic neuropathy (DN), characterized by nerve damage and neuropathic pain.[1]Almost half a billion people worldwide have diabetes, with the number projected to increase by 25% in2030 and 51% in 2045.This persistent high blood sugar can lead to various health complications.[2]The three main types of diabetes are Type 1, Type 2, Gestational diabetes.Type 1 diabetes is an autoimmune disease, An autoimmune disease results when the body's system fighting for infection.[3] The most common form of diabetes is type 2 diabetes. About 90 to 95 percent of people with diabetes havetype 2.[4] Some women develop gestational diabetes late in pregnancy. Although this form of diabetes usuallydisappears after the birth of the baby, women who had gestational diabetes have a 40 to 60 percent chanceof developing type 2 diabetes within 5 to 10 years.[5]Diabetic neuropathy is a major complication of diabetes mellitus and is the most common form ofneuropathy in the developed world. An internationally agreed simple definition of Diabetic neuropathyfor clinical practice is "The presence of symptoms and/or signs of peripheral nerve dysfunction in peoplewith diabetes after the exclusion of other causes." The neuropathic disorder includes manifestations in thesomatic and/or autonomic parts of the peripheral nervous system. It is not a single entity; it encompassesseveral neuropathic syndromes, by far the most

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common of which is diabetic neuropathy.[6] Current treatments for DNP includes Insulin aspart,Insulin detemir ,Metformin provide limited relief.[7] Herbal Medicine Natural remedies, specifically natural ones, are considered one of humanity's mosttraditional varieties of remedy humans had been eager to apply herbal remedies in latest years becausethey have fewer headaches and side consequences than artificial tablets.[8] *Colocaciaesculanta*is a plant traditionally used in various systems of medicine. Preliminary phytochemical investigations have revealed the presence of diverse bioactive compounds in its leaves, including alkaloids, Flavonoids, carbohydrates,Steroid, tannins, proteins. It shows Anti-inflammatory, Anticarcinogenic, wound healing, Antimicrobial,Antihepatotoxic, Antioxidant, Antihypertensive, Antidepressant, Anxiolytic, sedative, smooth muscle relaxant, Diarrhea,Arthritis, Internal hemorrhage.[9]

The phytochemicals present in *Colocaciaesculanta*may known for their antioxidant, anti-inflammatory, and analgesic properties which could potentially be beneficialin alleviating neuropathic pain associated with diabetes.

In this context the current study aims to evaluate the effect of MECE leaves on experimentally induced diabetic neuropathic pain in rats. The study assessed the impact of MECE on thermal hyperalgesia and motor coordination deficits.

II. PLANT PROFILE

Figure No. 1 :*Colocaciaesculanta*

Kingdom	Plantae
Division	Angiospermae
Class	Magnoliopsida
Phylum	Tracheophyta
Order	Arales
Genus	Colocacia
Species	Colocasiaesculanta

Botanical Classification of *Colocaciaesculanta*

III. MATERIALS AND METHOD

3.1 Materials

Chemicals and reagents : Petroleum Ether, Ethanol, Chloroform, Streptozotacin (STZ), Molish Reagent, Mayers Reagent, Sulphuric acid, Lead acetate, Ferric Chloride, Sodium Hydroxide, Hydrochloric Acid, Zinc, Citric acid, Sodium citrate, Glucose diagnostic Kit, Formalin 5% (50 uL).

Apparatus and Instruments: Analgesiometer, Rotarod Apparatus, Micro cooling Centrifuge.

3.2 Method

Procurement & Authentication of Leaves of *Colocasiaesculanta*

The plant was identified and authenticated by of VasantraoNaik Government College ofAgricultural Biotechnology, Waghapur road, Yavatmal.Leaves of *Colocasiaesculanta*were collected during October to December 2024 from

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villagen Borgaon, Nanded district, Maharashtra State, India.Voucher specimen was deposited at the institute.(No. VNCABT/Ytl/Hort/1599/2024 Date 29/11/2024)

Extraction of *Colocasiaesculanta*

Leaves of *Colocasiaesculanta*plant were, dried in shade and coarsely powdered and, thenprocess of removal of fat conducted in the glass jar with petroleum ether then, the defattedpowder was extracted in methanol by maceration. Then it was dried by evaporation in waterbath.

Phytochemical Screening

Freshly prepared Methanolic extract was subjected to phytochemical screening for the detectionof the various phytochemical active constituents.

Figure No. 2: Phytochemical Screening of *C. E* extract

3.3 Experimental Design

Experimental Animals

Male Wistar rats weighing between 180 - 220 grams were taken for the experiment. During thecourse of the experiment, they were kept in rooms with adequate ventilation that had atemperature of 24°C (75°F), a light/dark cycle lasting 12 hours, and a relative humidity of 55%.They were fed a regular pellet diet and access to water on an unlimited basis. The animals weregradually introduced to their new environment over the course of one week. All experimental procedures were approved by the Institutional Animal Ethical Committee (IAEC) with reference no. 650/PO/Re/S-2002/2025/CPCSEA/03 and conducted in accordance with the guidelines provided by the committee for the purpose ofcontrol and supervision of experiments on animals (CPCSEA), which is located in New Delhi,India.[10]

The animals was divided into five groups, with 6 animals in each group as follow:

Group 1 (Vehicle Control) :- Rats was received only normal saline solution.

Group 2 (Negative Control) :- Diabetic Neuropathy was induced in rats by usingStreptozotocin (60mg/kg) by intraperitoneal route.

Group 3 :-Diabetic Neuropathy induced rats were treated with C.E. (150mg/kg) for 14days.

Group 4 :-Diabetic Neuropathy induced rats were treated with C.E. (300mg/kg) for 14days.

Group 5 (Standard) :- Diabetic Neuropathy induced rats were treated with Metformin(25mg/kg) for 14 days.[11]

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Induction of Diabetic Neuropathy

Diabetes was induced by intraperitonial injection of STZ (60mg/kg) to overnight fasted rats.Diabetes was confirmed by the determination of fasting blood glucose level on the day 3 ofadministration with the help of Glucose diagnostic kit (Ambica diagnostics) showing fastingblood glucose levels above 200mg/dl.

Diabetic Neuropathy was confirmed after 4 weeks of induction of diabetes by following models:

a) Thermal Method

1. Tail flick model: The rat's tail was subjected towards heat generated by electrical stimulus.Cut off period will be set at max up to 10 sec. After day 28 of diabetic induction rats underNegative control group and treatment group was showing hyperalgesia characteristicconfirming neuropathy.

b) Mechanical Method

1. Swimming Endurance Test (SET) Model: Rats were immersed in water tank (diameter18 cm, height 40 cm) filled to a depth of 25 cm with water at 25°C. On the first experimentalday, rats were gently placed in the water for a 15 min period of habituation. On removalfrom the water, they were placed in a chamber box under a shed for 30 min to dry. The nextday, they were replaced in the tank and observed for 15min. During this period, the totaltime that spent immobile (i.e., making only the movements necessary to remain a float) ismeasured. Removal time was set at max 15-min. After day 28 rats was show decrease inmean swim time (MST) as compared to control group showing development of stress.[12]

2. Rota Rod Model: The animals were subsequently tested for muscle coordination on a Rotarod rotating at 25 rpm and the duration of stay on the rod was recorded. The mean fallingtime of Rats in different selected group will be noted after day 28 resulted into decreased infalling time as compared to Control group was showing loss of muscle strength.[13]

Statistical Analysis:

All data was expressed as the mean ± SEM. For statistical analysis of the data, group means wascompared by one-way analysis of variance (ANOVA) followed by Dunnett's test, $P<0.05$ wasconsidered significant.[14]

IV. RESULTS

4.1 Effect of MECE on Body Weight and Blood Glucose Levels:

Table No. 4.1 : Evaluation of Body Weight of Rats on day 0, 3, 28 and 42.

Group	Weight of rat on day 0	Weight of rat on day 3 (gm)	Weight of rat on day 28 (gm)	Weight of rat on day 42(gm)
Control	220±2.17	230±3.5	248±3.57	274±2.97
Negative control	215±1.12	165±15.27^{ns}	150±9.12*	140±10.22*
C.E(150mg/ kg)	210±1.18	164±20.12^{ns}	152±8.15$^{@@}$	142±9.28$^{@@}$
C.E(300mg/ kg)	212±2.12	170±9.12^{ns}	153±8.20$^{@@}$	145±8.17$^{@@}$
Metformin(25mg/kg)	218±2.18	220±8.17^{ns}	237±7.50$^{@@}$	256±9.10$^{@@}$

The results were expressed as Mean ± SD (n = 6),

*^{ns}= not significant, *p > 0.05, **p > 0.01, ***p < 0.0001 when compared to Control group of rats.*

^{ns}= not significant, $^{@}$p > 0.05, $^{@@}$p > 0.01, $^{@@@}$p < 0.0001 when compared to Negative Control group of rats.

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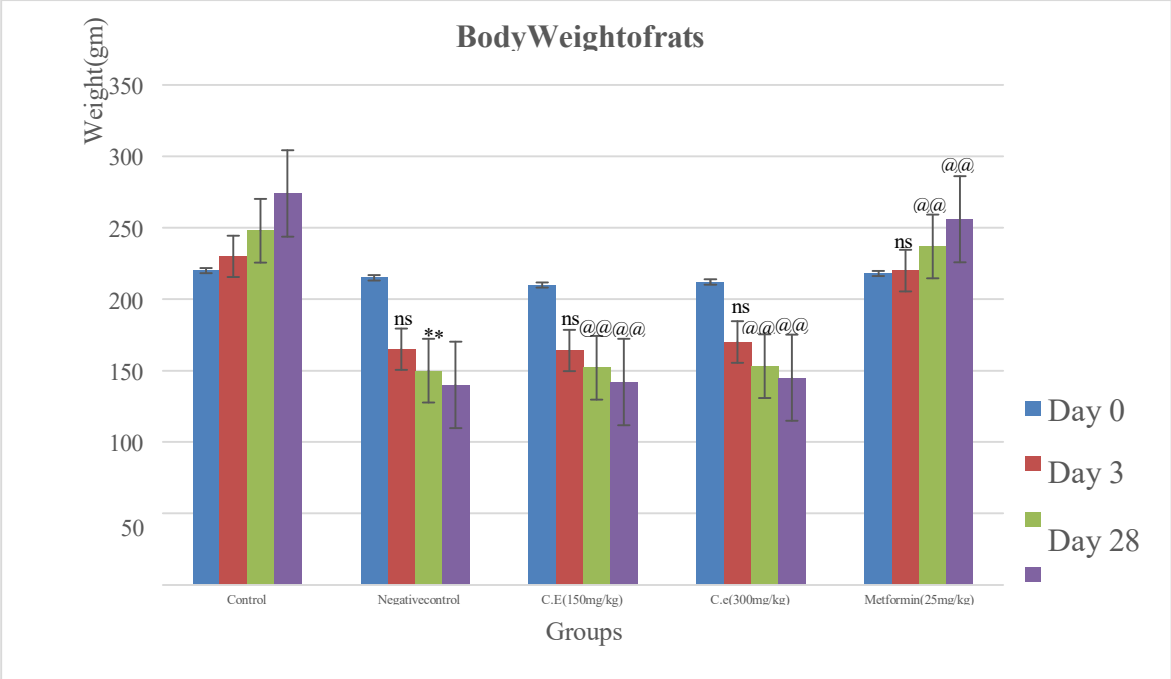

Figure No. 4.1 : Evaluation of Body Weight of Rats on day 0, 3, 28 and 42.

Table No. 4.1 and Figure No. 4.1 shows the effect of STZ on body weight of the rats on day 0, 3, 28 and 42. There was significant decrease ($p < 0.01$) in the body weight in all the groups of rats when compared to control group of rats on day 3, 28. This decrease in the body weight is due to diabetes in the rats. After confirmation of DN, rats were treated with MECEfor two weeks. After drug treatment, there was significant improvement in ($p < 0.01$) in the body weight in *Colocasiaesculenta*extract (300mg / kg), *Colocasiaesculenta* extract (150mg/kg) and Metformin (25mg/kg) treated group when compared to Negative control Group.

4.2 Estimation of blood glucose level

Table No. 4.2 : Evaluation of Blood Glucose Level of Rats on day 0, 3, 28 and 42.

Group	Bloodglucose levelofraton day0 (mg/dl)	Bloodglucose levelofraton day3 (mg/dl)	Blood glucose levelofratonday 28 (mg/dl)	Bloodglucose levelofraton day42 (mg/dl)
Control	90.48±2.21	98.24±8.15	93.44±6.12	98.37±7.32
Negativecontrol	92.85±1.17	$172.65±7.18^{ns}$	219.87±6.11*	233.59±9.24*
C.E(150mg/ kg)	80.89±1.15	$187.77±9.19^{ns}$	$149.37±7.55^{@@}$	$144.73±7.44^{@@}$
C.E(300mg/ kg)	87.98±2.15	$206.67±7.15^{ns}$	$185.27±10.77^{@@}$	$152.32±10.70^{@@}$
Metformin(25mg/kg)	95.15±2.17	$214.46±8.34^{ns}$	$177.33±9.28^{@@}$	$128.9±7.15^{@@}$

The results were expressed as Mean ± SD (n = 6),
*^{ns}= not significant, *p > 0.05, **p > 0.01, ***p < 0.0001 when compared to Control group of rats.*
^{ns}= not significant, $^{@}$p > 0.05, $^{@@}$p > 0.01, $^{@@@}$p < 0.0001 when compared to Negative Control group of rats.

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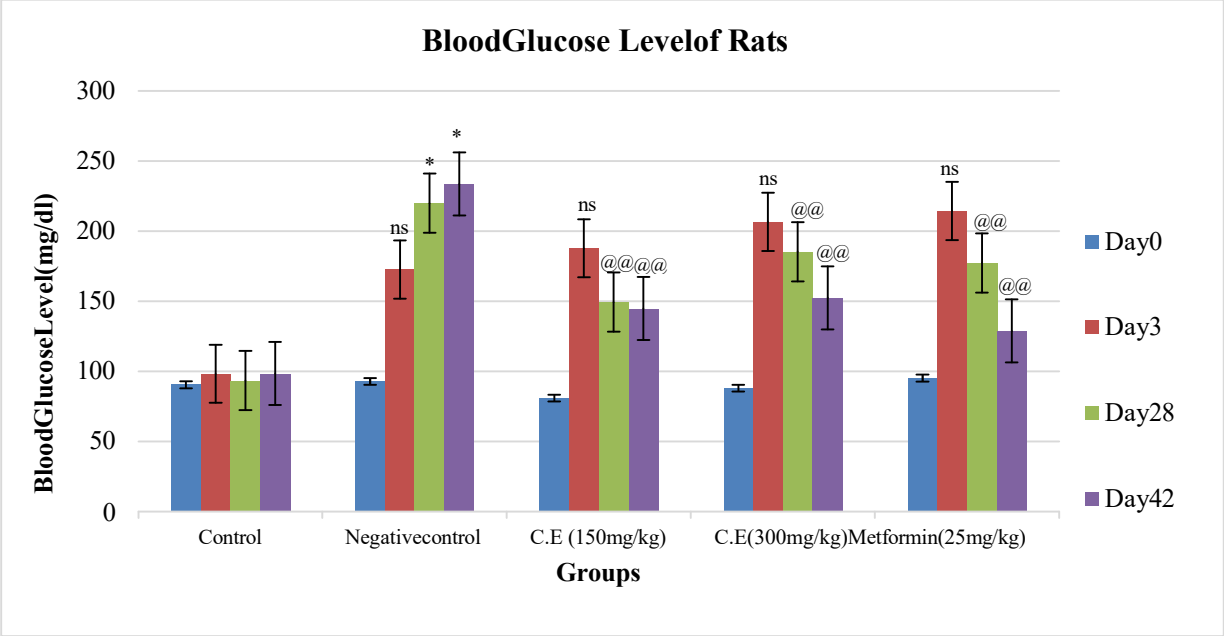

Figure No. 4.2 : Evaluation of Blood Glucose Level of Rats on day 0, 3, 28 and 42.

Table No. 4.2 and Figure No 4.2 shows the effect of STZ on Blood Glucose Level of the rats on day 0, 3, 28 and 42. There was significant increase ($p < 0.01$) in the Blood Glucose Level in all the groups of rats compared to control group of rats on day 3 and 28. This decrease in the Blood Glucose Level confirms due to diabetes in the rats. After confirmation of DN, rats were treated with MECE for two weeks. After drug treatment, there was significant decrease in ($p < 0.01$) in the Blood Glucose Level in *Colocasiaesculenta* extract (300mg / kg), *Colocasiaesculenta* extract (150mg / kg) and Metformin (25mg/kg) treated group when compared to Negative control Group.

4.3 Effect of MECE on Thermal Hyperalgesia (Tail Flick Test):

Table No. 4.3 : Tail Flick Response of Rats on day 0, 3, 28 and 42.

Group	Tail flick response of raton day 0 (insec)	Tail flick responseofrat on day 3(in sec)	Tail flick responseof raton day 28 (insec)	Tailflickresponse of rat on day 42 (in sec)
Control	6±1.17	5.84±1.12	5.96±1.10	5.92±2.10
Negativecontrol	5.95±1.15	$7.85±1.15^{ns}$	7.89±15.12*	5.20±1.18*
C.E(150mg/ kg)	5.45±1.19	$7.90±2.17^{ns}$	$7.85±16.18^{@@}$	$5.24±10.15^{@@}$
C.E(300mg/ kg)	5.83±1.12	$7.89±1.30^{ns}$	$7.80±17.12^{@@}$	$5.26±12.77^{@@}$
Metformin(25mg/kg)	5.9±1.16	$6.96±1.10^{ns}$	$6.15±15.18^{@@}$	$5.75±14.27^{@@}$

The results were expressed as Mean ± SD (n = 6),

*^{ns}= not significant, *p > 0.05, **p > 0.01, ***p < 0.0001 when compared to Control group of rats.*

^{ns}= not significant, $^{@}$p > 0.05, $^{@@}$p > 0.01, $^{@@@}$p < 0.0001 when compared to Negative Control group of rats.

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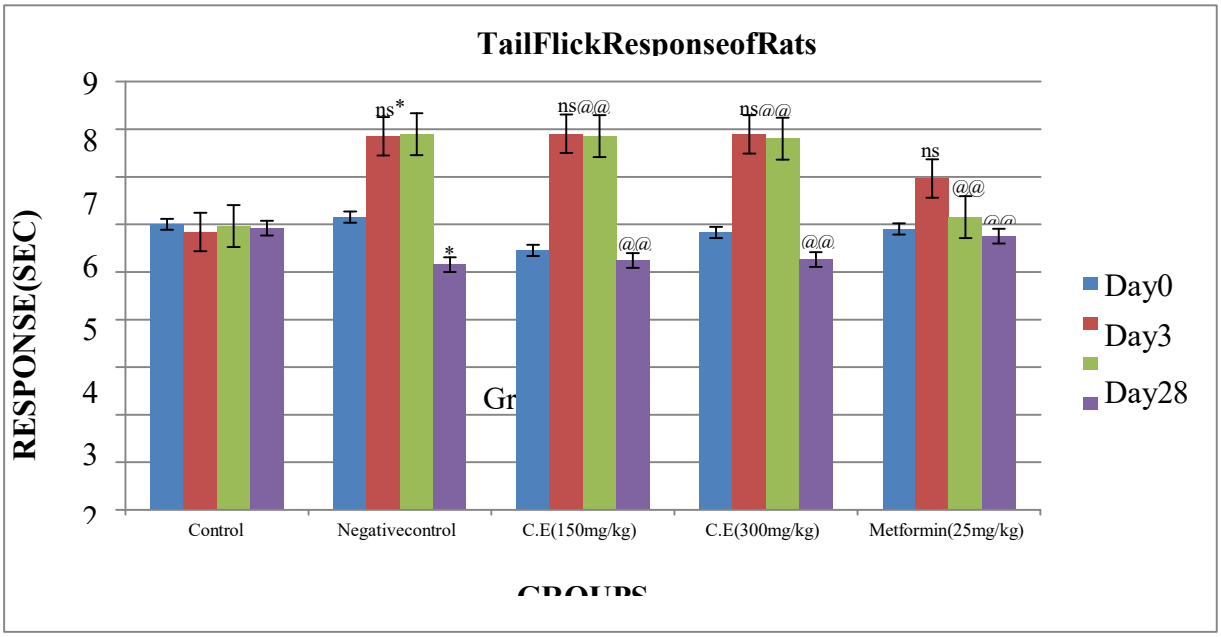

Figure No. 4.3 : Tail Flick Response of Rats on day 0, 3, 28 and 42.

Table No. 4.3 and Figure No 4.3 shows the effect of STZ on Tail Flick response of the rats on day 0, 3, 28 and 42. There was significant decrease ($p < 0.01$) in analgesic effect of rats compared to control group of rats. This decrease in analgesic effect confirm the hyperalgesia in the rats. After conformation of DN, rats were treated with MECE for two weeks. After drug treatment, there was significant improvement in ($p < 0.01$) in the Tail Flick Response in *Colocasiaesculenta*extract (300mg / kg), *Colocasiaesculenta*extract (150mg/ kg) and Metformin (25mg/kg) treated group when compared to Negative control Group.

4.4 Rota rod

Table No. 4.4 : Muscle Coordination Response of Rats on day 0, 3, 28 and 42.

Group	Meanfalling time of rat on day 0 (insec)	Meanfalling time of rat onday 3 (insec)	Mean falling timeofraton day28 (in sec)	Mean falling timeofraton day 42 (insec)
Control	70.15±1.13	45.65±5.12	58.32±7.40	67.78±6.78
Negativecontrol	71.18±1.05	49.27±6.40^{ns}	35.87±5.69*	27.68±4.98*
C.E(150mg/ kg)	69.85±1.11	55.58±7.12^{ns}	40.10±4.40$^{@@}$	50.15±3.58$^{@@}$
C.E(300mg/ kg)	69.45±1.14	59.68±5.17^{ns}	45.15±3.77$^{@@}$	53.16±3.45$^{@@}$
Metformin(25mg/kg)	72.15±1.12	60.15±4.57ns	50.15±4.95$^{@@}$	65.95±3.50$^{@@}$

The results were expressed as Mean ± SD (n = 6),
*^{ns}= not significant, *p > 0.05, **p > 0.01, ***p < 0.0001 when compared to Control group of rats.*
^{ns}= not significant, $^{@}$p > 0.05, $^{@@}$p > 0.01, $^{@@@}$p < 0.0001 when compared to Negative Control group of rats.

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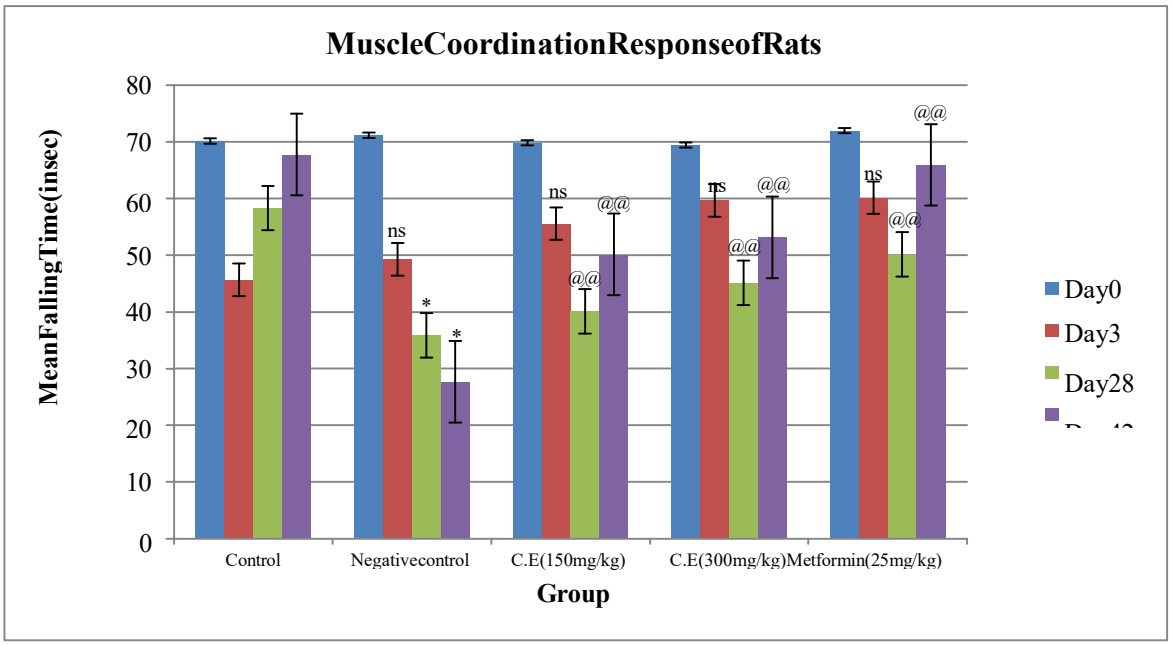

Figure No. 4.4 : Muscle Coordination Response of Rats on day 0, 3, 28 and 42.

Table No. 4.4 and Figure No 4.4 shows the effect of STZ on Muscle Coordination Response of the rats on day 0, 3, 28 and 42. There was significant decrease ($p < 0.01$) in Mean Falling Time of rats compared to control group of rats. This decrease in the muscle coordination confirms the loss of muscle strength in the rats. After confirmation of DN, rats were treated with MECE for two weeks. After drug treatment, there was significant improvement in ($p < 0.01$) in the Mean Falling Time in *Colocasiaesculenta* extract (300mg / kg), *Colocasiaesculenta* extract (150mg / kg) and Metformin (25mg/kg) treated group when compared to Negative control Group.

4.5 Swimming endurance test(set)

GROUPS	SET of rat on day 0 (in min)	SET of rat onday3(in min)	SET of rat on day 28 (in min)	SET of rato n day 42 (in min)
Control	11.5±1.19	10.80±2.15	11.24±2.45	11.40±1.95
Negativecontrol	12.2±2.01	09.80±1.50^{ns}	04.21±1.79*	03.62±1.17*
C.E(150mg/ kg)	10.3±2.12	09.00±1.78^{ns}	04.25±1.12$^{@@}$	09.12±1.78$^{@@}$
C.E(300mg/ kg)	11.2±1.15	09.04±2.15^{ns}	04.24±2.10$^{@@}$	08.40±2.25$^{@@}$
Metformin(25mg/kg)	11.6±1.12	10.15±2.59^{ns}	09.28±2.12$^{@@}$	09.31±2.11$^{@@}$

Table No. 4.5 : Swimming Endurance Test (SET) of Rats on day 0, 3, 28 and 42.

The results were expressed as Mean ± SD (n = 6),
*^{ns}= not significant, *p > 0.05, **p > 0.01, ***p < 0.0001 when compared to Control group of rats.*
^{ns}= not significant, $^{@}p > 0.05$, $^{@@}p > 0.01$, $^{@@@}p < 0.0001$ when compared to Negative Control group of rats.

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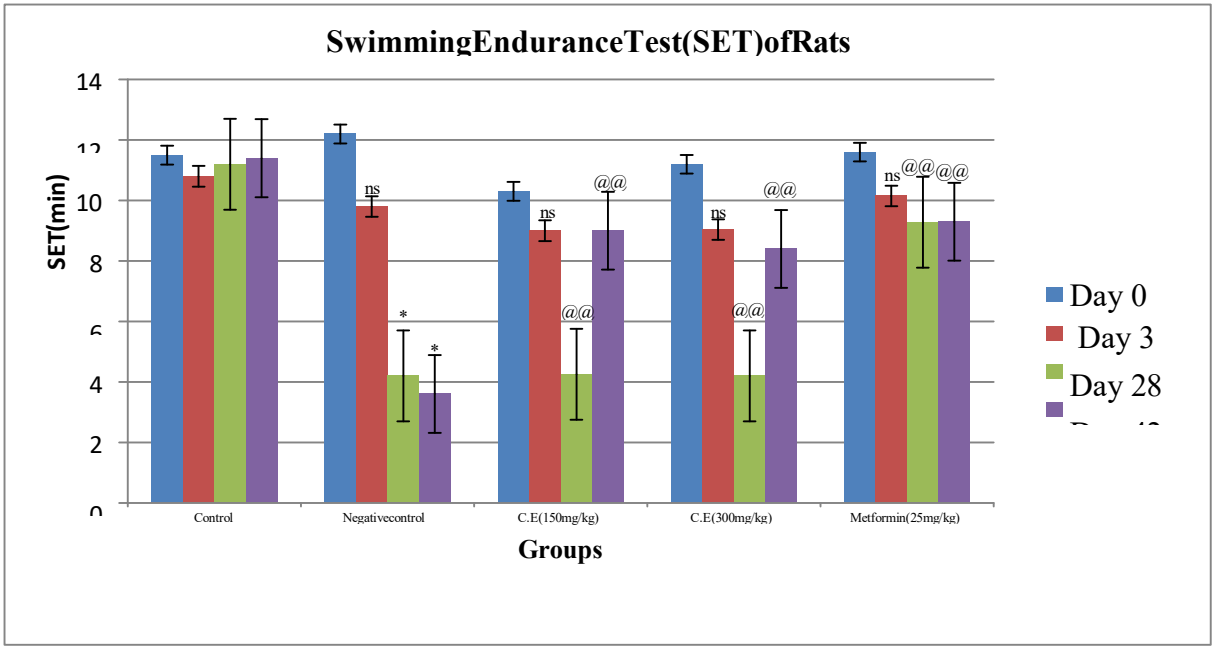

Figure No. 4.5 : Swimming Endurance Test (SET) of Rats on day 0, 3, 28 and 42.

Table No. 4.5 and Figure No 4.5 shows the effect of STZ on Swimming activity of the rats on day 0, 3, 28 and 42. There was significant decrease ($p < 0.01$) in immobility of rats compared to control group of rats. This decrease in the Swimming activity confirms the loss of muscle strength in the rats. After confirmation of DN, rats were treated with MECE for two weeks. After drug treatment, there was significant improvement in ($p < 0.01$) in the Swimming activity in *Colocasiaesculenta*extract (300mg / kg), *Colocasiaesculenta*extract (150mg / kg) and Metformin (25mg/kg) treated group when compared to Negative control Group.

V. DISSCUSION

Current study investigated the potential of MECE to alleviate diabetic neuropathic pain in STZ-induced diabetic rats. The successful induction of diabetes was confirmed by sustained hyperglycemia and a significant decrease in body weight in the STZ-treated group. Treatment with both low (150 mg/kg) and high (300 mg/kg) doses of MECE on day 28 and 42 demonstrated significant improvements in both thermal hyperalgesia and motor coordination deficits in diabetic rats. The observed effects of MECE could be attributed to the presence of various bioactive phytochemicals identified in the extract, including flavonoids, etc. Flavonoids are known for their potent antioxidant and anti-inflammatory properties.

VI. CONCLUSION

Present study reveals the activity of *Colocasiaesculenta*in Neuropathy induced by DM. The use of MECE minimized increased glucose level as well as showed improvement in Body weight in rats induced with DN.*Colocasiaesculenta*showed significant improvement in the muscle coordination activity, improved analgesic response in animal model than negative control groupHerewith we may conclude that MECE may be useful in treatment and management of Neuropathy induced by DM.

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