PLANTS WITH SKELETAL MUSCLE RELAXANT ACTIVITY: A REVIEW

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Introduction

- Skeletal muscle relaxants are of two different groups
- <u>Centrally acting muscle relaxants</u> used to reduce spasticity in a variety of painful conditions (chronic back pain and painful fibromyalgic conditions)
- <u>Neuromuscular blockers</u>-used during surgical procedures and in the intensive care unit (ICU) to produce muscle paralysis

- Skeletal muscle relaxants are used to treat muscle spasm and spasticity.
- Muscle sprains & muscle strains.
- The antispasticity agents baclofen, tizanidine, dantrolene, and diazepam-aid in improving muscle hypertonicity and involuntary jerks.
 - Antispasmodic agents, such as cyclobenzaprine, are primarily used to treat musculoskeletal conditions.
 - The side effects of antispasmodic & antispasticity agents cause them to be used with caution

Viola Betonicifolia



Common Name
 ✓ Arrowhead violet,
 ✓ Showy violet,
 ✓ Mountain violet

 Traditional use
 ✓ Epilepsy, insomnia, astringent, antipyretic, purgative
 ✓ Roots & flowers used in asthma, cough & cold

Other activity

 ✓ anxiolytic, sleep induction analgesic, antipyretic, anti inflammatory, anti convulsant ✓ Chimney test

Dose: VBME-300,400,500mg/kg i.p 4HC-10,20,30mg/kg i.p

Possible MOA:

Centrally acting skeletal muscle relaxant activity by interfering with GABA_A complex.



Effects of VBME (%) on muscle relaxation (Chimney test and Traction test).

Crown	Decoller	Chimney test (%)			Traction test (%)			
Group	Dose/kg	30 min	60 min	90 min	30 min	60 min	90 min	
Control	10 mL	0 ± 0.00	0 ± 0.00	0 ± 0.00	0 ± 0.00	0 ± 0.00	0 ± 0.00	
Diazepam	1 mg	$100 \pm 0.00^{***}$	$100 \pm 0.00^{***}$	$100\pm0.00^{\star\star\star}$	$100\pm0.00^{\star\star\star}$	$100 \pm 0.00^{***}$	$100 \pm 0.00^{***}$	
	0.3 g	10.12 ± 0.88	14.11 ± 0.97	11.09 ± 2.11	12.54 ± 1.10	15.23 ± 2.13	10.34 ± 1.90	
VBME	0.4 g	55.13 ± 1.23*	$61.56 \pm 0.65^{*}$	58.23 ± 0.56*	65.02 ± 0.23*	$72.12.04 \pm 0.56^{*}$	$68.04 \pm 0.34^{*}$	
	0.5 g	77.08 ± 0.11 <mark>**</mark>	80.76 ± 0.02**	80.55 ± 0.21**	75.05 ± 0.12**	78.03 ± 0.08**	77.67 ± 0.00**	

Effects of 4HC (%) on muscle relaxation (Chimney test and Traction test).

0	Dec. (he	Chimney test (%)			Traction test (%)		
Group	Dose/kg	30 min	60 min	90 min	30 min	60 min	90 min
Control	10 mL	0 ± 0.00	0 ± 0.00	0 ± 0.00	0 ± 0.00	0 ± 0.00	0 ± 0.00
Diazepam	1 mg	$100 \pm 0.00^{***}$					
	10 mg	0 ± 0.00					
4HC	20 mg	$15.13 \pm 1.34^*$	$20.21 \pm 1.35^*$	$20.45 \pm 0.44^{*}$	$4.50 \pm 1.67^{*}$	6.55 ± 1.22*	$3.54 \pm 1.89^{*}$
400	30 mg	30.34 ± 1.54**	37.33 ± 1.57**	35.45 ± 1.45**	25.34 ± 0.23**	27.04 ± 1.77**	26.78 ± 2.56**



Vicia Faba

Common Name
 ✓ Fava bean,
 ✓ Broad bean,
 ✓ Bell bean
 ✓ Field bean, tic bean

□Traditional use ✓As Food

□Other activity
✓ anti-parkinsonian

Part used for SMR activity

 Leaves, Seeds

 Extraction: Methanol; Soxhlet

 Phytochemicals: <u>Tanins</u>, saponins, steroids, alkaloids
 Animal used:

 Animal used:
 Animal Models used

✓ Rotarod

Dose: VFME 400mg/kg p.o. leaves + seeds 600mg/kg p.o.

Possible MOA:





(CONTROL: DISTILLED WATER)

S.NO	BODY WEIGHT(g)	BODY WEIGHT(g)	VOLUME OF DISTILLED WATER TO BE ADMINISTERED (ml)	FALL OFF TIME IN SECONDS
1	22	8.8	0.22	19
2	23	9.2	0.23	07
3	22	8.8	0.22	09

AVERAGE - 11.6 (Sec)

(TEST: METHANOLIC EXTRACT 400mg/kg)

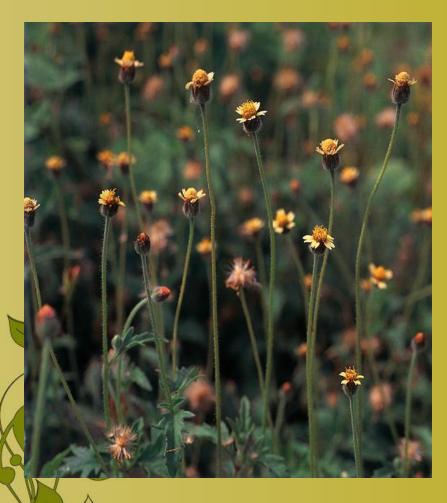
	1		00				
S.NO	BODY	DOSE	VOLUME OF EXTRACT TO	FALL OFF TIME IN			
	WEIGHT(g)	(mg/kg)	BE ADMINISTERED (ml)	SECONDS			
1	22	8.8	0.22	06 ±0.14***			
2	27	10.8	0.27	05±1.04			
3	21	8.4	0.21	02±0.74*			
	AVERAGE – 4.33 (Sec)						

(STANDARD: DIAZEPAM 4mg/kg)

S.NO	BODY	DOSE	VOLUME OF SELINE TO BE	FALL OFF TIME IN
	WEIGHT(g)	(mg/kg)	ADMINISTERED (ml)	SECONDS
1	21	0.084	0.21	04±0.61***
2	24	0.096	0.24	02±0.15**
3	20	0.080	0.20	02±0.42*
			AVED COD A	2.2.10 N

AVERAGE – 2.66 (Sec)

Tridax procumbens



Common Name ✓ Coat buttons, ✓ Mexican daisy, ✓ Hindi: Gavpattha ✓ Telugu: Ravanasuruditalakai

 □Traditional use
 ✓ Bronchial catarrh, dysentery, diarrhoea, restoring hair
 □Other activity
 ✓ Wound healing, anti microbial, anti diabetic, hepatoprotective ■Part used for SMR activity ✓ Leaves

Extraction: Aqueous; (Maceration; Percolation)

 Phytochemicals: luteolin, quercetin, glucoluteolin, isoquercetin
 Animal used:

✓ Albino mice & wistar rats

Animal Models used
✓ Rotarod/ Inclined plane.

Dose: 4.2, 8.2 & 12.6mg/kg i.p

Possible MOA: -





Effect of aqueous extract of TP on muscle grip strength using Rota rod						
Treatment (mg/kg)	Fall off time (sec)		% Decrease			
(i.p.)	Before	After	70 Decrease			
Diazepam (0.3)	67.4±3.53	11.2±3.08***	79.4±3.17			
TP (4.2)	63.6±2.94	23.2±1.14***	66.8±2.47			
TP (8.4)	115.8±1.53	68.6±3.17***	41.2±3.21			
TP (12.6)	54±2.38	35.4±3.82***	38.8±1.39			

Senna occidentalis



Common Name ✓ Stinking weed, ✓ Coffee senna, ✓ Coffee weed

Traditional use (powdered leaves)
✓ Analgesic, antimicrobial, Insecticidal, febrifuge, vermifuge,purgative, epilepsy

Other activity (leaves) Anti carcinogenic, anti mutagenic, anti inflammatory, anti rheumatic, anti plasmodial. Part used for SMR activity
 Seeds
 Extraction: Ethanol; Maceration
 Phytochemicals: <u>Anthraquinones</u>, cardiac gycosides, alkaloids, saponins, tannins, flavanoids.

❑Animal used:
 ✓Wistar rats
 ❑Animal Models used
 ✓Rotarod
 ✓Actophotometer

Dose: 50, 100, 200mg/kg p.o
Toxicity study: LD₅₀ :3250mg/kg bw

Possible MOA:





Effects of ESESO on Skeletal Muscle Relaxant Activity in Wistar Rats

S.No	Treatment	Dose	Mean fall-off time in min			% Decrease in fall-off time in 10 mints	
	1 cutilitie	(mg/kg)	Before After Treatment		After	After	
			Treatment	30	60	30	60
1	Diazepam	4	15.23±2.14	4.01±0.76*	2.83±0.45*	73.67	81.42
2	ESESO	250	14.13±3.88	4.13±0.65*	7.76±0.80*	70.79	69.27
3	ESESO	500	13.80±1.34	4.26±0.79*	5.80±0.96*	69.13	57.97

Saraca indica



Common Name
✓ Ashoka
✓ Sita ashoka

□Traditional use
✓ Digestion, Antimicrobial,
Astringent, Menorragia.

Other activity

✓ CNS depressant, diuretic, antimicrobial, cytotoxic, oxytocic, antiulcer, antidiabetic, antioxidant □ Part used for SMR activity ✓ Leaves **Extraction:** Methanol; soxhlet Phytochemicals: Flavanoids, saponins, triterpinoids, tanins, glycosides, steroids, alkaloids. **Animal used:** ✓ Albino mice Animal Models used ✓ Rotarod

Dose: 200mg/kg p.o.

Possible MOA: Flavanoids , saponins & triterpinoids are thought to potentiate GABAergic inhibition.





	Effect of Methanolic Extract of Saraca indica Linn. on Mice by Rotarod Method.						
S.No	Treatment	Dose mg/kg body weight	Locomotion test				
1	Control (Distilled water)	5ml/kg	93.35±4.07				
2	Diazepam	4	50.86±2.88***				
3	Methanolic Extract	200	74.75±1.73**				
4	P value		<0.0001				
5	F value		48.69				

Parthenium hysterophorus



Common Name ✓ Congress grass

Traditional use
 Tonic, febrifuge,
 emmenagouge, analgesic in
 neuralgia.
 Root decoction used for
 dysentery.

Other activity: Antiamebic, antitumor, trypanocidal, antimalarial Part used for SMR activity

 Leaves

 Extraction: Methanol; Soxhlet
 Phytochemicals: anthraquinones, saponins, steroids, tanins, reducing sugars

❑Animal used:
 ✓Albino mice
 ❑Animal Models used
 ✓Rotarod
 ✓Traction test

Toxicity study: LD₅₀ 50-300mg/kg Dose: 3, 5mg/kg p.o

Possible MOA: Depolarizing neuromuscular junction blocking effect





DURATION OF TIME SPEND ON ROTAROD

Group	Dose	0 minutes	30 minutes
Control	Saline soln.	328.17 ± 1.62	322.7±24.85
Diazepam	10 mg/kg i.p.	340.50 ±18.93	104.8±2.85**
MEPH	5 mg/kg p.o.	342.23 ±18.60	189.5±41.57*
MEPH	3mg/kg p.o.	342.50 ±12.23	201.00±32.45*

Nerium oleander



Common Name
 Kaner, Arali
 Potentially toxic in all parts

□Traditional use

✓ Variety of skin disorders,
herpes, leprosy, tumors,
abortifacient
✓ Leaves: cardiotonic,
antibacterial, cutaneous
eruptions, diuretic, snakebite

Other activity: Anti tumor, inhibit FGFR2 Part used for SMR activity

 Leaves, flower

 Extraction: Aqueous; Soxhlet
 Phytochemicals: anthraquinones, saponins, steroids, tanins, flavonoids

❑Animal used:
 ✓Albino rats
 ❑Animal Models used
 ✓Rotarod
 ✓Actophotometer

Toxicity study: safe upto 2000mg/kg Dose: 100, 200mg/kg p.o

Possible MOA: Augmenting GABA, CNS depressant action.



Effect of AENOF on locomotor activity in actophotometer and muscle coordination on the Rotarod apparatus

Group (n=5)	Actophotometer score in 5 min before	After 60 min of administration	Percentage of reduction	Time spent on revolving rod in Rotarod apparatus (s)
Group I (control) -NS 10 ml/kg	153.2±2.58	-	0	318±17.72
Group II (standard) -Diazepam10 mg/kg	217.8±7.67	13.33±2.17**	93.87	15.17±2.24**
Group-III -AENOF 100 mg/kg	194.5±4.66	41±1.58**	78.86	186.8±8.04**
Group-IV -AENOL 200 mg/kg	180±5.78	25.4±2.07**	86.11	35.4±3.84**

**P<0.000, All values are expressed as mean±SD. SD=Standard deviation, AENOF=Aqueous extract of Nerium Oleander flowers

Effect of AENOF on locomotor activity in actophotometer after giving the extract directly into the muscle

Group (n=3)	Actophotometer score before 5 min	Actophotometer score after 5 min	After 30 min of administration	Percentage of reduction after 30 min	Р
Group I (control) -distilled water 10 ml/kg	167.2±3.38	166.8±3.32	164.6±3.28	1.55	0.613
Group-II -AENOF 100 mg/kg	191.8±4.36	190.2±4.29	188.8±4.20	1.57	0.706
Group-III -AENOL 200 mg/kg	182.1±4.19	180.8±4.06	179.1±3.92	1.65	0.680

P>0.05, all values are expressed as mean±SD. SD=Standard deviation, AENOF=Aqueous extract of Nerium Oleander flowers

Cinnamomum zeylanicum





□ Common Name
✓ Cinnamon

Traditional use

- ✓ Cookery-condiment
- ✓ Musculoskeletal disorders
- Cinnamon oil used for cold flu, aching muscles.

Other activity:
 ✓ Nrf2 – ARE pathway-Antioxidant action.
 ✓ Anti melanoma activity.
 ✓ NFKB/ NF-KB

 Part used for SMR activity
 Bark (Inner bark)
 Extraction: Aqueous; Soxhlet
 Phytochemicals: volatile oils, cinnamonaldehyde, eugenol, transcinnamic acid, proanthrocyanidins

❑Animal used:
 ✓ Albino rats
 ❑Animal Models used
 ✓ Rotarod
 ✓ Actophotometer

Toxicity study: safe upto 2000mg/kgDose: 50,100, 200mg/kg p.o

Possible MOA: -





Groups		Time spent on revolving rod in		
		60 minutes after administration	% of Reduction	Rotarod apparatus (in seconds
Group I (control) NS 10 ml / kg	158.3 ± 60.89		0	99.67 ± 1.74
Group II (standard) Diazepam10 mg / kg	215.7 ± 70.12	9.33 ± 8.45***	96.06	12 ± 0.73**
Group-III AECZB 50 mg / kg	163.5±1.72	$45.5 \pm 1.25^{***}$	72.39	82.17 ± 0.60*
Group-IV AECZB 100 mg / kg	203.2 ± 1.79	$32.83 \pm 1.30^{***}$	83.85	$30.33 \pm 1.20^{**}$
Group-V AECZB 200 mg / kg	193.5 ± 1.60	14.67 ± 1.06***	92.41	$19.17 \pm 0.60^{**}$

Effect of AECZB on the locomotor activity on the actophotometer and muscle Coordination on the rotarod apparatus

AESCZB-Aqueous extract of S Cinnamomum Zeylanicum. All values are Mean ± SD, n = 6, *P < 0.05, **P < 0.01, ***P < 0.000 when compared with the control

Hibiscus rosa-sinensis



Common Name ✓ Red hibiscus ✓ China rose ✓ Japapushpam

□Traditional use
 ✓ Hair care preparation
 ✓ Shoe shining
 ✓ Anti solar agent

Other activity: Abortifacient, Dentifrice, expectorant, antipyretic, anti inflammatory, analgesic, anti estrogenic. Part used for SMR activity✓ Leaves

 Extraction: Methanol; Soxhlet
 Phytochemicals: Flavanoids (hibiscitin), phenolic content, terpinoid like sitosterol, camphesterol

Animal used:
✓ Albino rats
Animal Models used
✓ Rotarod
✓ Dose: 200mg/kg p.o

Possible MOA: -



Skeletal Muscle Relaxant effect of MEHR on rat using Rota-rod model									
For Skelatal muscle relaxant: Rota rod model (time required to fall down)									
Sr. No.	Group	Control (seconds)	Standard (seconds)	Test (seconds)					
1	Head	240	5	17					
2	Tail	250	6	15					
3	Back	260	8	21					
4	head tail	250	5	17					
5	back tail	240	7	18					
6	No mark	240	4	17					
Average		246.66	5.83	17.5					
SD		8.16	1.47	1.97					
SEM		3.34	0.60	0.80					
variance		66.66	2.16	3.9					

Mikania scandens



Common Name

✓ Climbing hempwood
✓ Climbing hempvine
✓ Louse plaster

□Traditional use
 ✓ Cover crop, livestock
 fodder, butterfly garden
 ✓ Gastric ulcer, wounds,
 Insect bites & stings



Part used for SMR activity✓ Ariel parts

 Extraction: Hydroalcoholic .
 Phytochemicals: flavonoids, steroids, tanins, saponins, sugar



❑Animal used:
 ✓ Albino mice
 ❑Animal Models used
 ✓ Rotarod
 ❑Toxicity study : safe upto 2000mg/kg p.o
 ❑Dose: 250, 500mg/kg i.p

Possible MOA: -

Treatment	Dose (mg/kg)	Mean fall off time (seconds)			% decrease in fall off	
		Before	After treatment		time	
		treatment	30 min	60 min	After 30 min	After 60 min
Diazepam	4	15.23 ± 2.14	4.01 ± 0.76*	2.83 ± 0.45*	73.67	81.42
HAMS	250	14.13 ± 3.88	4.13 ± 0.65*	7.76 ± 0.80*	70.77	45.08
HAMS	500	13.80 ± 1.34	4.26 ± 0.79*	5.80 ± 0.94*	69.13	57.97

Effect of HAMS on muscle relaxant activity in mice

Data are expressed as mean \pm SEM (n=6); *P<0.001 compared with control (mice before treatment), assessed by paired Student's 't' test

Moringa oleifera





Common Name ✓ Drumstick tree ✓ moringa ✓ Horse radish tree

□Traditional use
 ✓ Purification of water
 ✓ Handwashing
 ✓ Forage for livestock
 ✓ anthelminthic

Other activity: Anti inflammatory, antioxidant, antimicrobial, hypocholestrol, antiobesity, CNS depressant action Part used for SMR activity✓ Leaves

 Extraction: Ethanol ; Soxhlet
 Phytochemicals: Flavonoids saponins, tanins, phenolic acids.

❑Animal used:
 ✓Albino rats
 ❑Animal Models used
 ✓Rotarod

Dose: 50, 100, 200, 400mg/kg p.o

Possible MOA: -



 EEMO showed significant (p<0.05) progressive decrease in time of fall from rotarod with increase in dose.

Phyllostachys bambusoides



Common Name ✓ Giant timber bamboo ✓ Japanese timber bamboo

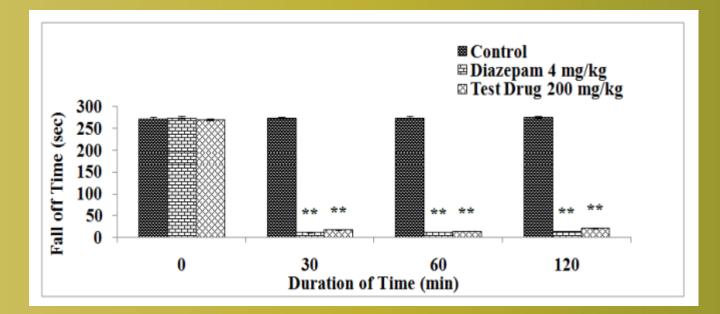
□Traditional use
 ✓ Anti inflammatory,
 ✓ Anti pyretic,
 ✓ diuretic

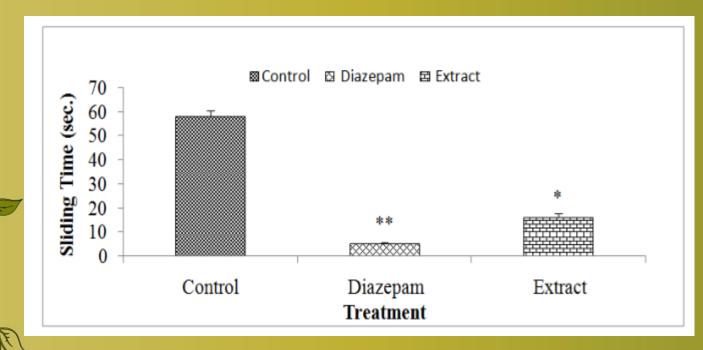
 Other activity: Hypertension, antioxidant, antimicrobial, anticancer
 Used for treating cardiovascular
 disorders & arteriosclerosis. Part used for SMR activity✓ Leaves

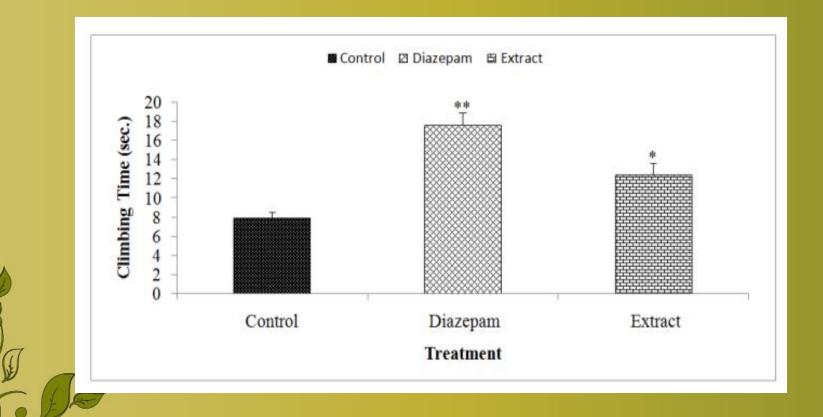
 Extraction: Chloroform; Soxhlet
 Phytochemicals: Flavanoids glycosides, tannins, proteins, carbohydrates

□Animal used:
✓ Wistar rats
□Animal Models used
✓ Rotarod
✓ Inclined screen test
✓ Climbing test
□ Toxicity studies: toxicity at 2000mg/kg p.o
□ Dose: 200mg/kg p.o



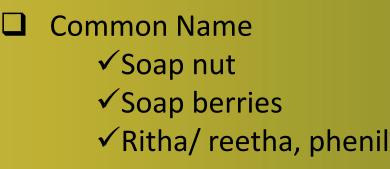






Sapindus trifoliatus





□Traditional use
✓ Fruits/ berries natural sufactant-soap, kill lice
✓ Spermicidal, emetic, expectorant, epilepsy

Other activity: antiepileptic, used in migraine.

Part used for SMR activity✓ Pericarp

Extraction: Aqueous; Soxhlet Phytochemicals: <u>Saponins</u>, anthraquinones, tannins, isoflavanoids **Animal used:** ✓ Albino mice Animal Models used ✓ Rotarod ✓ Actophotometer Toxicology: non toxic upto 2000mg/kg p.o Dose: 200mg/kg p.o

Possible MOA: -Possibly Isoflavanoids bind to GABA/BZD receptor complex in brain.





Effect of AEST on locomotor activity in actophotometer and muscle coordination in rotarod apparatus

Groups n=10	Actophotometer score in 5 min before	After 60 min of administration	% of Reduction	Time spent on revolving rod in rotarod apparatus(sec)
Group I(control) NS 10ml/kg	158.3 ± 60.89		0	100 ± 10.54
Group II(standard) Diazepam10mg/kg	215.7 ± 70.12	9.33 ± 8.45***	96.06	12.2 ± 3.58**
Group-III AEST 50mg/kg	165.3 ± 13.98	47.33 ± 9.13***	71.37	82.8 ± 22.14*
Group-IV AEST 100mg/kg	218 ± 25.04	33 ± 22.57***	85.11	32.3 ± 15.07**
Group-V AEST 200mg/kg	198.3 ± 76.2	14.67±14.14***	87.73	20.3 ± 2.94**

AEST-Aqueous extract of Sapindus trifoliatus. All values are Mean \pm SD, n = 10, *P < 0.05, **P < 0.01, ***P < 0.000 when compared with control.

Conclusion

- Many traditional plants with significant SMR activity.
- Traditional medicine--screening and bio prospecting large number of new drug leads.
- Active principle and its mechanism of action.
 - More studies needed in this direction.

References

- 1. Naveen M, Mohammad S, Harron K, Achyut A and Khalid MK. Muscle Relaxant and Sedative-Hypnotic Activities of Extract of Viola betonicifolia in Animal Models Supported by Its Isolated Compound, 4-Hydroxy Coumarin. Journal of Chemistry 2013; Vol 2013:p 1-6.
- 2. Kalakonda R and Kaidiri SK. Screening of skeletal muscle relaxant activity of plant vicia faba. Int J Pharm 2013; 4(1):p 237-40.
- Kumbhar S.P, More R.R, Burande M.D, Waghmare P.V. Evaluation of Skeletal Muscle Relaxant Activity of Tridax procumbens Linn. in Mice and Rat. International Journal of Toxicological and Pharmacological Research 2014; 6(4):p 102-105.
 - Cletus A.U, Francis J.I, Monday I.E, Didigwu J.C, Nathaniel S.M. Investigating antinociceptive and skeletal muscle relaxant properties of Ethanol seed extract of senna occidentalis linn. (Fabaceae) in wistar rats. International Journal of Research in Pharmaceutical and Nano Sciences 2013; 2(4):p 485 - 494.

Talever S, Snigdha G, Milind P, Akansha S. Neuropharmacological Screening of Saraca Indica leaves. Guru Drone Journal of Pharmacy and Research 2014; 2(2): p 30 -37.

- Urmilesh J, Prites J.C, Rajesh J.O and Tushar T.S. Skeletal muscle relaxant activity of methanolic extract of Parthenium hysterophorus L. leaves in swiss albino mice. International journal of pharmacy & life sciences 2011; Vol 2(11):p 1211-13.
- 7. Jayasree T, Maulik P, Ubedulla S, Harini K and Shankar J. Evaluation of skeletal muscle relaxant activity of aqueous extract of Nerium oleander flowers in Albino rats. Indian J Pharmacol 2015;47:409-13.
- Jayasree T, Kavitha R, Chandrasekhar N, Saequa S. Evaluation of centrally acting skeletal muscle relaxant activity of aqueous extract of Cinnamomum zeylanicum bark in albino mice 2012; Vol1(2): 94-8.
- Ganatra TH, Joshi UH, Patel MN, Desai TR and Tirgar PR. Study of Sedative, Anxiolytic, CNS – Depressant and Skeletal Muscle Relaxant Effects of Methanolic Extract of Hibiscus Rosa-Sinensis on Laboratory Animals. J Pharm Sci & Res. Vol 3(4): 1146-1155.

10. Protapaditya D, Sangita C, Priyanka C, Sanjib B. Neuropharmacological

properties of Mikania scandens (L.) Willd (Asteraceae).

Adv Pharm Technol Res 2011; Vol 2(4): 2559.

THANK YOU

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