Neuropharmacological actions of Panchagavya formulation containing *Emblica officinalis* Gaerth and *Glycyrrhiza glabra* Linn in mice

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A panchagavya Ayurvedic formulation containing *E. officinalis*, *G. glabra*, and cow’s ghee was evaluated for its effect on pentobarbital-induced sleeping time, pentyleneetrazol-induced seizures, maximal electroshock-induced seizures, spontaneous motor activity, rotarod performance (motor coordination) and antagonism to amphetamine in mice. The formulation (300, 500 mg/kg, po) produced a significant prolongation of pentobarbital-induced sleeping time and reduced spontaneous locomotor activity. The formulation also significantly antagonised the amphetamine induced hyper-locomotor activity (500, 750 mg/kg, po) and protected mice against tonic convulsions induced by maximal electroshock (500, 750 mg/kg, po). The formulation slightly prolonged the phases of seizure activity but did not protect mice against lethality induced by pentyleneetrazol. The formulation did not show neurotoxicity. The results suggest that the panchagavya formulation is sedative in nature.

Keywords: Anticonvulsants, Neuropharmacological activity, CNS, Sedative, Panchagavya, *Emblica officinalis*, *Glycyrrhiza glabra*.

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Medicinal plants have played a key role in world health. Herbal drugs have been used since ancient times as medicines for the treatment of range of diseases. Herbal medicinal preparations are still popular in developing countries inspite of great advances observed in modern medicine in recent decades. Panchagavya is a term used in Ayurveda to describe the five important cow products, viz. milk, curd, ghee, urine and dung. These components are used either alone or in combination with other herbs for treatment of several diseases. The panchagavya based polyherbal formulations, viz. Haridradi Ghrita and Ashtamangal Ghrita showed immunomodulatory activity and Jatyadi Ghrita was found to be anti-inflammatory agent. Amalkadi Ghrita (AG) is also one of the Panchagavya herbal formulation mentioned in Ayurveda for the treatment of epilepsy and disorders of liver. The ingredients of Amalkadi Ghrita (AG) are *Emblica officinalis* Gaerth (10 g), *Glycyrrhiza glabra* Linn (10 g) and cow’s ghee (80 g). *Emblica officinalis* had been reported for its immunomodulatory, antioxidant, gastroprotective, hypolipidemic and antimutagenic activities. *Glycyrrhiza glabra* is well-known for its anti-inflammatory agent, anti-ulcerogenic and anticonvulsant action and is useful in liver disorders. Therefore in the present study AG has been evaluated for its neuropharmacological activity.

Amalkadi Ghrita (AG)—The formulation Amalkadi Ghrita (AG) was obtained as a gift sample for research from Go-Vigyan Anusandhan Kendra, Nagpur, India. The formulation was prepared by an expert Ayurvedic practitioner. The formulation was used as received.

Animals—Male Swiss albino mice weighing 25-30 g were used. The animals were housed in groups of 6 per cage at 25 ±1°C and 55 ±5% RH. A 12:12 dark:light cycle was followed during the experiments and the experiments were carried out during the light portion (0800-1600 hrs). The animals were fed with standard pellet diet (Lipton India Ltd. Mumbai) and water ad libitum. The Institutional Animal Ethics Committee approved the protocol for study.

Assessment of behavioural effect—The behavioural effects of AG (100, 300 and 500 mg/kg body weight, po) were assessed as per Irwin et al. After 2 hr of
treatment the animals were observed for loss of righting reflex, depression, twitches, lacrimation, passivity and tremors. Also dose up to 2 g/kg body weight was administered to observe mortality after 24 hr.

**Pentobarbital-induced sleeping time**—Mice(24) were divided into four groups of 6 each and treated as follows; Group I animals received pentobarbital sodium (45 mg/kg body weight, ip) only. Animals in groups II, III and IV received AG (100, 300 and 500 mg/kg body weight, po) and after 30 min they were administered pentobarbital sodium (45 mg/kg body weight, ip). The time elapsed between loss and recovery of the righting reflex was taken as sleep duration and recorded for control and pretreated animals.

**Effect on locomotor activity**—Spontaneous locomotor activity was recorded using an activity cage (Actophotometer, Centronics, Bombay) with automatic counting of animal movements on the cage floor. The animals were divided in 4 groups (n=6) and treated with either vehicle or AG (100, 300 and 500 mg/kg body weight, po) respectively. The locomotor count for each animal was recorded for 5 min at 30 min interval for 2 hr.

**Maximum electroshock (MES)-induced seizures**—The formulation AG was fed orally to groups of mice (n=6) in doses ranging from 300-750 mg/kg body weight 60 min before the application of electric shock (42 mA, 0.2 sec) using corneal electrodes\textsuperscript{18}. The duration of hind leg extension was noted.

**Pentylenetetrazole (PTZ)-induced seizures**—The formulation AG did not protect mice against all phases of seizure activity defined by tonic, clonic, hind paw extension and lethality, but altered the time of onset

<table>
<thead>
<tr>
<th>Parameters</th>
<th>AG (mg/kg)</th>
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<tbody>
<tr>
<td>100</td>
<td></td>
</tr>
<tr>
<td>300</td>
<td></td>
</tr>
<tr>
<td>500</td>
<td></td>
</tr>
<tr>
<td>Loss of righting reflex</td>
<td>-</td>
</tr>
<tr>
<td>Depression</td>
<td>2/6</td>
</tr>
<tr>
<td>Twitches</td>
<td>-</td>
</tr>
<tr>
<td>Lacrimation</td>
<td>-</td>
</tr>
<tr>
<td>Passivity</td>
<td>1/6</td>
</tr>
<tr>
<td>Tremors</td>
<td>-</td>
</tr>
</tbody>
</table>

The data shows the number of mice having abnormal signs compared to the control mice. (n=6)
of clonic phases induced by PTZ. The data were not significant (data not shown).

Motor co-ordination—Pretreatment of AG up to 750 mg/kg, po dose did not exhibit any effect on motor coordination as determined by rota-rod performance in mice (data not shown).

Amphetamine antagonism—AG in doses 500 and 750 mg/kg, po antagonized significantly the amphetamine induced hyper-locomotor activity in mice (Fig. 3).

**Discussion**

In the present study the neuropharmacological activity of a polyherbal formulation ‘Amalkadi Ghrita’ (AG) was assessed. The formulation was found to be safe up to 2 g/kg body weight dose orally. No mortality was observed in 24 hr. The activity was CNS inhibitory in nature as evident by the behavioural assessment of AG. AG showed decreased locomotor activity and rearing in mice as well as hyporeactivity of animals towards external stimuli like touch and noise. The decrease in rearing and locomotion indicated depressive effect on CNS. The results of AG treatment on pentobarbitone induced sleep and spontaneous locomotor activity were corroborated with behavioural assessment. The formulation significantly prolonged the pentobarbitone induced sleeping time. The prolongation of pentobarbitone induced sleeping time may be attributed to inhibition of pentobarbitone metabolism or central mecha-

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**Table 2**—Effect of Amalkadi Ghrita (AG) on MES induced seizures in mice

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Duration of tonic extensor phase (sec) ± SE</th>
<th>Incidence of convulsions</th>
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<tbody>
<tr>
<td>Vehicle</td>
<td>15.66 ± 1.37</td>
<td>6/6</td>
</tr>
<tr>
<td>AG 300</td>
<td>13.66 ± 0.693</td>
<td>6/6</td>
</tr>
<tr>
<td>500</td>
<td>11 ± 0.67</td>
<td>5/6</td>
</tr>
<tr>
<td>750</td>
<td>8.25 ± 0.53*</td>
<td>4/6</td>
</tr>
</tbody>
</table>

*P values: *<0.01; †<0.05; One Way ANOVA followed by (Dunnett’s test)
nisms involved in the regulation of sleep. The potentiation of pentobarbitone induced sleep and decrease in spontaneous locomotor activity suggest central depressant effect. The above suggestion was strengthened by the antagonism showed by AG to amphetamine stimulated locomotor effect. The amphetamine is a CNS-stimulant and antagonism to amphetamine stimulated hyperlocomotor activity indicates CNS inhibitory effect of AG. The formulation did not show motor deficit activity, which suggests that AG may act centrally as neurosedative. AG showed reduction in tonic extensor phase in maximal electroshock-induced seizures. The antiepileptic drugs that block MES-induced tonic extension may act by blocking seizure spread. The AG however slightly prolonged onset of action but did not afford any protection against PTZ induced convulsions in mice in the doses tested. The formulation may be tested at higher dosage or by other models for screening of anticonvulsant efficacy and to reveal exact mechanisms of action of AG on CNS. In conclusion it can be said that the panchagavya herbal formulation AG has CNS-inhibitory effect in mice and may be useful as a therapeutic tool and adjuvant in supportive therapy of epilepsy and other CNS disorders.

References


