Preliminary Acute And Subacute Toxicity Study Of Some Homoeopathic Drugs*

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Summary

13 homoeopathic drugs were studied for their preliminary acute and subacute untowards and toxic effects in 181 albino mice. Of 13 homœopathic drugs, Calitropis gigantea and Acidum formicum (1 : 9 dilutions) were found to be quite toxic leading to death of all mice. On the other hand, Solanum xanthocarpum drug prepared by percolation technique had protective effect against alcohol lethality. Cannabis indica, Cannabis sativa, Azadirachta indica and Cassia fistula had tranquilizing effect of varying degree whereas Aegle folia, Hydrocotyle asiatica, Ficus religiosa, Tylophora indica, Thymol (3X) and Cuprum oxydatum nigrum had no observable effects on mice in the doses employed.

It is suggested that cure may be exercised in prescribing homoeopathic drugs in low potencies particularly in infants and in children and Solanum xanthocarpum drug may be taken up for its proving for its protective effect against alcoholic toxicity by clinicians.

Introduction

Every new drug or new formulation of already established drug has to be thoroughly examined in animals for their untowards and toxic effects and their efficacy in producing biological and therapeutic effects for its superiority in relation to already established drug for getting approval by the Government of respective country to evaluate its therapeutic efficacy in human volunteers and introducing it into the market for public use. As the provings of homoeopathic drugs are essentially carried out in healthy human volunteers, it was decided to explore the untowards and the toxic effects of homœopathic drugs in animals as a part of biological screening of drugs besides the drugs requested by Head Quarter for toxicological studies.

Materials and Methods

In the present paper, the study carried out on 13 homoeopathic drugs for preliminary acute and subacute untowards and toxic effects during last 3 years on 181 albino mice of either sex (25-35 gb. wt) is reported. These mice were fed adlibitum Hindustan Lever feed and water. They were divided into groups and subgroups of varying numbers depending on the number of mice available and drugs evaluated at a particular time. The tincture of homoeopathic drugs (1X) were either administered as such or were diluted to 1 : 9 with distilled water before use; whereas homoeopathic drugs made in lactose were suspended first in distilled water for convenience of oral administration.Control mice were given either alcohol or lactose in equivalent volume and concentration of homoeopathic drug under study. The drugs were administered daily in 2 or 3 divided doses for duration of 5-10 days and the influence of homoeopathic drugs were observed daily between 10.00 to 17.00 hr. for the duration of drug treatment and for a week thereafter on the following parameters.

1. Central nervous system : Alterness, passivity, excitation, sedation, spontaneous motor activity, motor incoordination, equilibrium maintenance, posture and stereotype.

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2. Behaviour effects : Biting, fighting, facial movements and coupling,
3. Rate and depth of respiration (gross effects),
4. Heart rate and its force of contraction (gross effects),
5. Mortality and
6. Any other untoward effects observable during the period of drug treatment.

Autopsy of dead mice was conducted for gross examination of visceral organs to know the possible cause of death.

DRUGS

Acidum formicum, Aegle folia, Calotropis gigantea Cassia fistula, Cuprum oxydatum nigrum, Hydrocotyle asiatica and Tylophora indica (all 1X) and Thymol (3X) homoeopathic drugs were supplied by Head quarters whereas Azadirachta indica, Cannabis sativa, Cannabis indica, Ficus religiosa and Solanum xanthocarpum (all 1X), homoeopathic drugs were prepared in our unit from the raw material collected from local areas.

Results

The detailed reports of 13 homoeopathic drugs for acute and subacute toxicity study are summarized in Tables 1-5. Of the 13 homœopathic drugs, Calotropis gigantea and Acidum formicum (1 : 9 dilution of 1X in distilled water) were found to be quite toxic resulting into the death of all the mice during 6 days period. Details of symptoms are reported in Table 1. Whereas Cannabis indica, Cannabis sativa, Azadirachta indica and Cassia fistula produced drowsiness which was more pronounced in Cannabis group. These mice responded well to tactile stimuli indicating that these drugs had tranquilizing effect rather than sedative effects in these doses (Table 2). Aegle folia, Ficus religiosa, Tylophora indica and Thymol were practically devoid of any observable effect on any of the parameters. (Tables 4 & 5). In case of Cuprum oxydatum nigrum though one mice died but its death could not be related to the drug because no mortality was noticed in those mice who received higher concentration of drug. Such mortality was also noted in control mice given lactose alone in same doses (Table 4).

On the other hand homoeopathic drug prepared from Solanum xanthocarpum (1X) either from berries or whole plants by percolation, appeared to have protective effects against alcoholic lethality as 0.1 ml of (69% v/v) strong alcohol thrice daily for the period of 6 days resulted into death of 5 mice out of 6, whereas no mortality was noted in mice given Solanum xanthocarpum tincture prepared from berries and only one died out of 6 mice given Solanum xanthocarpum tincture prepared from whole plant by percolation. The protective effect against alcohol lethality was less marked with tincture prepared by maceration technique (Table 3). Physico-chemical studies carried out in our laboratory also indicate that the tincture prepared by percolation technique had higher alkaloid content and extractive values implying that alkaloid present in Solanum xanthocarpum appears to have protective effect against alcohol.

Discussion

The root bark and milky juice of Calotropis gigantea, commonly known as 'AK' or 'Mudar' in India, have been reported to be useful in the treatment of syphilis, leprosy, dysentery, elephantiasis and other ailments (Chopra, 1958). Duncan (1829) recognized the emetic action of the root bark and recommended as substitute for Ipecacuanha in medicine. Owing to their toxic effects, same have been used for homicidal and suicidal purposes. (Warden and Waddel, 1885). On the other hand Formic acid has been reported to be quite irritant leading to blindness due to optic nerve damage. The present study further confirmed that as a homœopathic drug when administered to the mice in a dose of 0.1 ml./10g. body wt. thrice daily for a period of 6 days in a dilution of 1 : 9 of the tincture both Calotropis gigantea and Acidum formicum are quite toxic resulting into death of all animals. On the other hand, Solanum xanthocarpum commonly known as 'Kantkari' in Hindi speaking areas reported to be useful in asthma, cough, catarrhal affections of the lungs, fever, flatulence and pain in the chest in ancient times, was found to have protective effect against alcohol lethality in mice when administered as its tincture. The tranquilizing effect of Cannabis is well known and has also been observed in present study with its tincture administered in dilution of 1 : 9 with distilled water. Such tranquilizing effect was also noted with Cassia fistula and Azadirachta indica.

In conclusion we suggest that care may be exercised while prescribing Calotropis gigantea and Acidum formicum to the patients and preferably they should not be given in form of tincture and should be prescribed in dilutions only, whereas Solanum xanthocarpum drug may be taken up for its proving towards alcohol intoxication by homoeopathic physician.

TABLE–1

Preliminary acute and subacute toxicity study of Homœopathic drugs

Name of Drug	Mice used (sex)	Volume given/dose*	Dilution of drug	No. of times dose given/day	Duration of drug given in days	Dead/alive ratio	Pharmacological or untoward effects if any and autopsy findings
Calotropis gigantea (1X)	6 (BS)	0.1 ml	1:9	2	6	6/0	Mice showed laboured breathing and gasping. Heart slowed but contracted forcefully. On autopsy, heart appeared small in size. Lungs and viscera congested.
Acidium formicum (1X)	6 (BS)	0.1 ml	1:9	2	6	6/0	Mice became drowsy. On autopsy, stomach was full of food; intestines contained watery fluid. There was thinning of stomach and intestinal walls implying irritant nature.
Alcohol (8% v/v)	6 (BS)	0.1 ml	—	2	6	0/6	Mice were quite active. Even drowsiness was not noticed.

BS indicates mice of both sexes; and dilution of drug referred to the dilution of drug in distilled water.
* Volume given 0.1/g. b. wt. orally.

TABLE–2

Preliminary acute and subacute toxicity study of Homœopathic drugs.

Name of Drugs	Mica used (sex)	Volume given/dose	Dilution of drug	No. of times dose given/day.	Duration of drug given in days	Dead/alive ratio	Pharmacological or untoward effects if any and autopsy findings
Cassia fistula (1X)	6 (BS)	0.1ml*	1 : 9	2	6	0/6	Slight drowsiness was observed in later part of drug treatment.
Azadirachta indica (1X)	6 (BS)	0.1ml*	1 : 9	2	6	0/6	Mice became drowsy after 3-4 days. Responded to tactile stimuli. No motor incoordination and ataxia.
Cannabis sativa (1X)	8 (M)	0.1ml	1 : 9	3	6	0/8	Mice became drowsy; Eyelids half closed. Responded to tactile stimuli.
Cannabis indica (1X)	8 (M)	0.1ml	1 : 9	3	6	0/8	As above
Alcohol							
a) (7% v/v)	8 (M)	0.1ml	—	3	6	0/8	Mice were quite active. Even drowsiness was not observed.
b) (8% v/v)	6 (BS)	0.1ml*	—	2	6	0/6	

M indicates male mice, BS indicates both sexes of mice. Dilution of drug referred to dilution of drug in distilled water.* Represents volume of dose given/10 g. b. wt. of mice orally.

TABLE-3

Preliminary acute and subacute toxicity study of Homoeopathic drugs.

Name of Drugs	Mice used (M)	Volume given/dose	No. of times dose given/day	Duration of drug given in days	Dead/alive ratio	Pharmacological effects or any other effects noted if any.
Solanum xanthocarpum (1X)						
a) Prepared by percolation :						
i) Whole plant	6	0.1ml.	3	6	1/5	Solanum xanthocarpum drug (1X) prepared by percolation had protective effect against alcoholic lethality more than the drug prepared by maceration method as only 1 out of 12 mice died in percolation group in comparison to 5 out of 12 mice in maceration group.
ii) Berries	6	0.1ml.	3	6	0/6	
b) Prepared by maceration:						
i) Whole plant	6	0.1ml.	3	6	3/3	
ii) Berries	6	0.1ml.	3	6	2/4	
Alcohol (69% v/v)	6	0.1ml.	3	6	5/1	

M indicates male mice.

TABLE-4

Preliminary acute and subacute toxicity study of Homoeopathic drugs

Name of Drugs	Mice used (BS)	Volume given/dose	Dilution of drug	No. of times dose given/day	Duration of drug given in days	Dead/alive radio	Pharmacological effects or any other effects noted if any.
Cuprum oxydatum	5	0.2 ml	1 : 4	2	5	0/5	—
nigrum	5	0.4 ml	1 : 4	2	5	1/4	
(1X)	5	0.4 ml	1 : 2	2	5	0/5	
Thymol	5	0.2 ml	1 : 4	2	5	0/5	—
(3X)	5	0.4 ml	1 : 4	2	5	0/5	
	5	0.4 ml	1 : 2	2	5	0/5	
Lactose	5	0.2 ml	1 : 4	2	5	0/5	—
	5	0.4 ml	1 : 4	2	5	1/4	
	5	0.4 ml	1 : 2	2	5	0/5	
Hydrocotyle	5	0.2 ml	1 : 1	2	5	0/5	—
asiatica	5	0.4 ml	1 : 1	2	5	0/5	
(1X)	5	0.4 ml	—	2	5	0/5	
Alcohol	5	0.2 ml	1 : 1	2	5	0/5	—
(60% v/v)	5	0.4 ml	1 : 1	2	5	0/5	
	5	0.4 ml	—	2	5	0/5	

BS indicates mice of both sexes;

Dilution of drug referred to dilution of drug in distilled water.

TABLE-5

Preliminary acute and subacute toxicity study of Homoeopathic drugs

Name of Drugs	Milce used (M)	Volume given/dose	No. of time dose given/day	Duration of drug given in days	Dilution of drug	Pharmacological effects or any other effects noted if any.
Aegle folia	4	0.25 ml	2	8	0/4	—
	4	0. 5 ml	2	2	0/4	
Ficus religiosa	4	0.25 ml	2	8	0/4	—
	4	0.50 ml	2	2	0/4	
Tylophora indica	4	0.25 ml	2	8	0/4	—
	4	0. 5 ml	2	2	0/4	
Alcohol (5% v/v)	4	0.25 ml	2	8	0/4	—
	4	0. 5 ml	2	2	0/4	

M indicates male mice.

@ 20 ml. of homoeopathic drug (1X) was evaporated to dryness; dissolved in 1 ml of strong alcohol and the final volume was made to 20 ml by distilled water.

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