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EXPERIMENTAL EVALUATION OF DUGDHIKA (EUPHORBIA PROSTRATA W. AIT) FOR THE TREATMENT OF 'TAMAKA SVASA' (BRONCHIAL ASTHMA)

GOPAL DUTT SHARMA AND S. N. TRIPATHI*

Dept. of Ayurvedic Medicine, Kasturba Medical College, Manipal – 576 119, Karnataka, India.

** Dept. of Kaya chikitsa, Institute of Medical Sciences, Banaras Hindu University, Varanasi – 221 005, India.*

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ABSTRACT: *The plant Dugdhika belongs to the family Euphorbeaceae and is found all over India up to the height of 6000 ft. Various workers have proved it beneficial for the treatment of Bronchial asthma, on the basis of their clinical and experimental studies conducted on the mixture of two plants i.e. Euphorbia thymifolia Linn and Euphorbia prostrate W. Ait, taken by the name of Dugdhika. Again, both the plant species have two ecotypes – Red & Green. The present study has been exclusively conducted on the red ecotype of E. Prostrata W. Ait.*

The paper deals with certain experimental studies on water soluble fraction of total alcoholic extract of the plant, to evaluate its efficacy and the mode of action in the treatment of Bronchial asthma. The study reveals that the drug causes relaxation of smooth muscles by virtue of which the spasm of Bronchial muscles during an acute attack of bronchial asthma, is relieved and thus exhibits its beneficial effect.

INTRODUCTION

'Tamaka Svasa' is a disease which is prevalent all over the world. The word Tamaka Svasa appears synonymous to Bronchial asthma as the clinical features of both have great resemblance. Moreover, all the recognized etiological factors of the later are also included in the "Nidana" of the former since the ancient time. The disease is known to have multiple etiology but the exact etiopathogenesis is not yet fully established. It is a chronic disease characterized by episodes of exacerbations and ameliorations leading to progressive damage of the lungs followed by frequent, severe and prolonged paroxysmal attacks of dysponoea and Vice – Versa. The incidence of asthma is continuously increasing and an increase of 16% has been reported in G. Britain just in the last decade, whereas the incidence in India is approximately 2%3.

As far as the treatment of Tamaka Svasa (Bronchial asthma) is concerned, it is still a challenge to the entire medical profession in

spite of the extensive researches all over the world. Modern medicine provides only palliative treatment as neither the relief is long lasting or the disease cured. Moreover, such treatment for a longer duration is always likely to give raise other complications. Hence, the search for better, safe and curative anti-asthmatic drugs is imminent.

Dugdhika has been used traditionally since ancient times in the treatment of Tamaka Svasa. By the name Dugdhika, two plants Euphorbia prostrate W. ait and Euphorbia thymifolia Linen are used. Morphologically both these plants are very much similar each having two ecological types of red and the green microscopically however, they are different. The ovary and fruits of E.thymifolia are hairy throughout while in E. prostrate hairs are present only along the ribs (Angles). On the basis of morphologic similarity both of these plants are widely used by popular traditional physicians and sages at several religious centers and institutions in India for the treatment of Bronchial asthma. So far only few scientific clinical studies have been conducted either on the mixture of the above two species and their ecotypes[1] or on the red ecotype of both the plants[2]. These studies have claimed it useful in bronchial asthma. However, the only experimental evaluation conducted so far pertained to the mixture of both the species with their ecotype[1]. Therefore, there is a need to separately establish the efficacy in either of the plants or in their particular ecotypes. Thus, the present study is exclusively conducted on the red ecotype of Euphorbia prostrate to evaluate its efficacy for the treatment of Bronchial asthma experimentally.

MATERIALS AND METHODS

Preparation of Alcoholic extract:

Sun – dried total plants of E. Prostrata (red ecotype) were taken, identified microscopically and coarse powdered. This powder was placed in a filter paper thimble and put in soxhlet extractor using alcohol as a solvent. The alcohol soluble contents of the drug were extracted with the usual procedure. The alcohol of the soxhlet was kept just on boiling for 30 hours as 26 hours were required for solvent (alcohol) coming through the soxhlet siphon to become colourless. The extract thus obtained was heated on a water bath to evaporate the solvent completely, (1gm. of alcohol ext. = 4.5 gms. of crude dried drug) and the semi solid total alcoholic extract thus obtained was divided into the water insoluble and the water soluble fractions. The present study was conducted on the water soluble fraction employing the following four experiments.

Experiment No.1:

Effect of drug on bronchospasm is histamine aerosol chamber.

Materials and Methods

The experiment was a little modified form of Sigemund & Graner method4. Nine healthy guinea pigs (each weighing between 250 – 300 gms). were taken and put in the airtight histamine aerosol chamber one at a time to test their normal response to histamine vapours. The vapours of 1% histamine dihydrochloride having the pressure of 290 + 2 m.m. of Hg, sprayed in the chamber-with the help of an atomizer and air compressor. The stop watch was started with the start of the spray and stopped immediately as the animal fell to one side which indicated the end point and the time for each guinea pig was thus noted. The animal was removed immediately from the chamber and kept in a separate cage in

open air. Only those animals were included in the experiment which took between 1 to 10 minutes for developing the complete bronchospas, i.e. falling down to one side. Only one animal took more than 10 minutes to fall down and therefore was rejected and the remaining eight were divided into two groups namely (A) Experimental group & (B) the control group.

In the experimental group 5 animals were placed and each was given 750 mg / kg of Dugdhika extract by intraperitoneal injection with strict aseptic precautions. In the control group, the other three animals were taken and each, was given 2 c.c. of sterile normal saline intra – peritoneally.

The animals of both the groups were allowed a period of about 2 hours after the injection for proper absorption of the test drug / N. saline and then each animal was again exposed to the vapours of 1% histamine solution at the pressure of 290 ± 2 m.m. of Hg individually by putting them in the histamine aerosol chamber and the time of each guinea pig as it fell down to one side was noted.

Observations

The observations are given in Table No.1 and 2.

Experiment No. 2

The effect of test drug on isolated rat ileum.

TABLE – 1

Showing effect of Dugdhika extract on histamine induced bronchospasm in guinea pigs (Experimental group)

Animal Name	Time of developing spasm prior to administration of test drug	Time of developing spasm after 2 hours of administration of test drug
A	90 Sec.	174 Sec.
B	77 Sec.	120 Sec.
C	65 Sec.	110 Sec.
D	69 Sec.	180 Sec.
E	80 Sec.	93 Sec.
Mean	76.2 Sec.	135.4 Sec.
S. D.	9.783	46. 366
S. E.	4.375	20.736

t	-	3.3352
p	-	<0.01

TABLE – 2

Showing time taken to produce bronchospasm in guinea pigs before and after the injection of N. saline (control group)

Animal Name	Time of developing spasm prior to injection	Time of developing spasm after 2 hours of injection
M	69 Sec.	74 Sec.
N	72 Sec.	70 Sec.
O	108 Sec.	110 Sec.
Mean	83 Sec.	84.67 Sec.
S. D.	± 21.7	± 21.338
t	-	0.1019
p	-	>0.05

Materials and Methods

The experiment was conducted by following Van Rossametal method[5]. Healthy albino rats of 100 to 200 gms. of weight were selected and fasted for 20 to 24 hours. A rat was taken, sacrificed by head blow and dissected. About 2.5 cms. Long piece of ileum was then taken out, cleaned of its lumen contents and mesentric flaps and kept in oxygeneated tyrode physiological solution for rat at a temperature of 37^{o}C. Both ends of this ileum were tied with separate pieces of threads keeping its lumen patent. One end of this piece was then tied with the hook of airating tube of isolated organ bath and the other free thread of the another free end was tied to the universal lever recording its movements on the kymograph. The tyrode solution was then filled in the isolated organ tube up to the mark and find but steady stream of oxygen was allowed to pass through the airating tube. The temperature of the water surrounding the organ tube was maintained at 37 ± 0.5^{o}C.

The tissue was checked for its normal response by adding aquous solutions of acetyl choline and adrenaline in the tyrod solution of organ tube. Then, the test drug was added in gradually increasing concentrations and the tissue response was recorded.

The experiment was conducted separately on duodenums / ileums of four albino rats.

The changing of tyrode solution in the organ tube, was done frequently after getting the response of each drug till normal tissue movements were observed.

Observations:

As it is evident from the Fig. No.2, the drug in the concentrations of 0.5 mg / ml insignificantly increases the movements of the smooth muscles but in higher concentrations (1 mg / ml above) produces definite relaxation in the smooth muscles of intestine.

Experiment No.3

The effect of the test drug on the isolated rabbits ileum / jejunum and its preventive action against histamine and acetyl choline induced spasms.

Materials and Methods:

The experiment was conducted on the basis of Finkelmen[6] method. Healthy rabbits were selected and kept on fasting except water for 24 hours prior to starting the experiment. The rabbits were sacrificed by head blow. A mid abdominal incision was made through the abdominal muscles and the abdominal wall was opened. The jejunum / ileum was identified and freed from its mesentric attachements and lumen contents and placed in oxygenated mammalian Ringer's solution at a temperature of $37 \pm 0.5^{o}C$.

About 2 cms long piece of jejunum/ileum was taken and mounted in isolated orgin tube of organ bath as in the experiment No.2 with a slight change i.e. the organ tube was filled with mammalian Ringer's solution and the movements of the tissue were recorded on the smoked paper of the kymograph.

The tissue was tested for its normal response with aquous solution of acetyl choline and isoprenaline. The response of the test drug was then studied. The tissue was washed by changing solution of organ tube 3 to 4 times before adding a new drug or the different concentrations of the same drug. The test drug showed significant relaxant action as evident from figure no.3. The Beta blocker propanolol and alpha Blocker priscol were tried separately as well as together to block the relaxant action of the drug.

To investigate the preventive action of the test drug against histamine and acetyl choline induced spasm of smooth muscles, the concerning spasmogen was given first to see its response and the tissue washed 5 times and then the test drug in the concentration it showed relaxant action, was added with the spasmogen and the movements of the tissue were recorded.

Observation:

The trial drug in the concentrations of 0.5 mg/ml and 0.75 mg/ml showed insignificant actions on the rabbits jejunum / ileum but definite relaxant action in the concentrations of 1mg/ml and in higher concentrations as evident from the figure no.3. The relaxant actions of the drug could not be blocked by only alpha blockers or beta blockers or by both together. The drug also successfully prevented the spasmogenic action of histamine dihydrochloride and acetyl choline chloride as evident from the figure no.3.

Experiment No.4

The effect of test drug on carbachol induced spasm of guinea pig tracheal chain.

Materials and Methods:

A healthy guinea pig was taken and sacrificed by head blow. Trachea was extracted and cut down transversely in 6 equal pieces while keeping the trachea in Vandyke hasting's solution[7]. All these pieces were tied together with thread as per the method of Castillo and Debear[8] and thus making a chain keeping the cartilage free ends of each piece to the same side. One end of this chain was tied with the oxygen delivery tube and another with the recording lever after placing the tracheal chain in isolated organ tube containing Vandyke hasting's solution[7]. A very fine and slow stream of oxygen was allowed to pass in the solution of organ tube. The mounted tracheal chain thus prepared was allowed to relax for one and a half hour while frequent changing of solution was continued. The temperature of the water bath was kept at 37 ± 0.5^{o}C.

The normal tone of the tracheal chain was recorded and then spasm was produced in the tracheal chain by adding carbachol. After recording the spasm on the kymograph the test drug was added in graded concentrations and the responses were recorded.

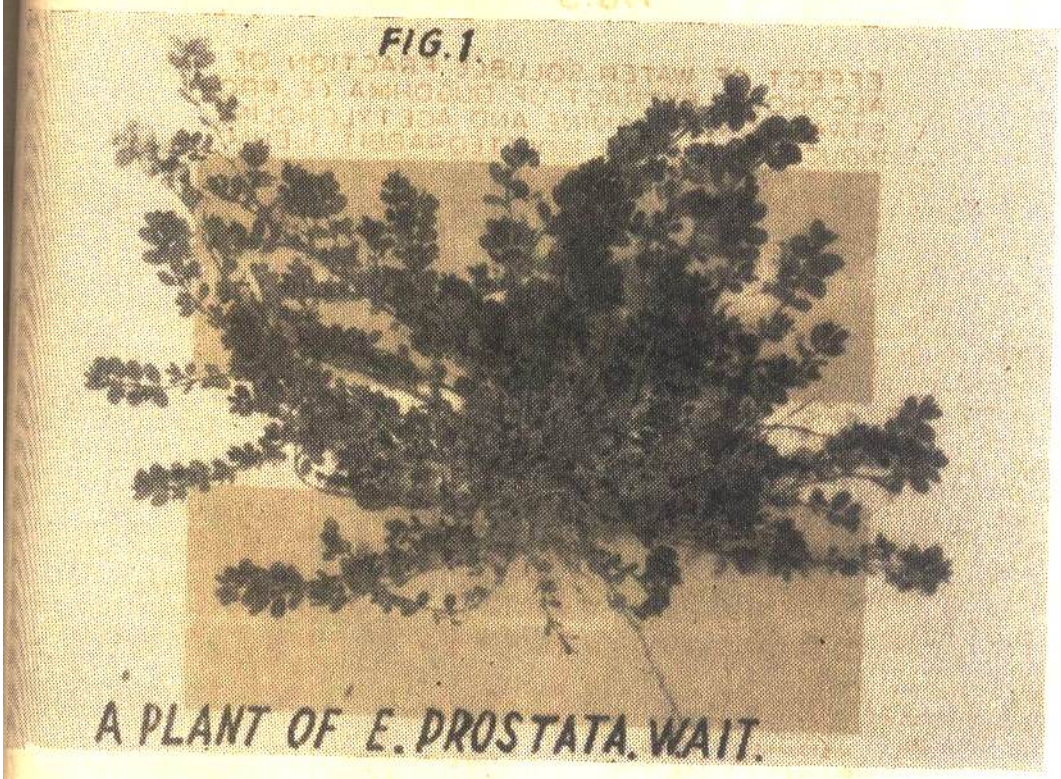
Observations:

The administrations of carbachol (50 mg/ml) produced gradual spasam in tracheal chain as evident from the Fig. No.4. The drug was then administered in the concentration of 5 mg/ml and a mild relaxation in the spasm of tracheal chain was observed. On increasing the concentration of the drug to 15 mg/ml, complete relaxation in the (spasm of) tracheal chain was observed.

In order to confirm our observations again, the spasm in same tracheal chain was again produced by carbachol and then the drug was added in the same concentrations (15 mg/ml). The same relaxant (spasmolytic) action of the drug was observed.

In order to check the response of the tracheal chain to the known relaxants spasm was produced again and then pirbuterol – a specific Beta – 2 agonist was added. The normal (expected) relaxant response was observed.

FIG.1.



A PLANT OF E. PROSTATA. WAIT.

FIG.2

EFFECT OF WATER SOLUBLE FRACTION OF ALCOHOLIC EXTRACT OF DUGDHIKA (E. PROSTRATA) ON ISOLATED RAT ILEUM

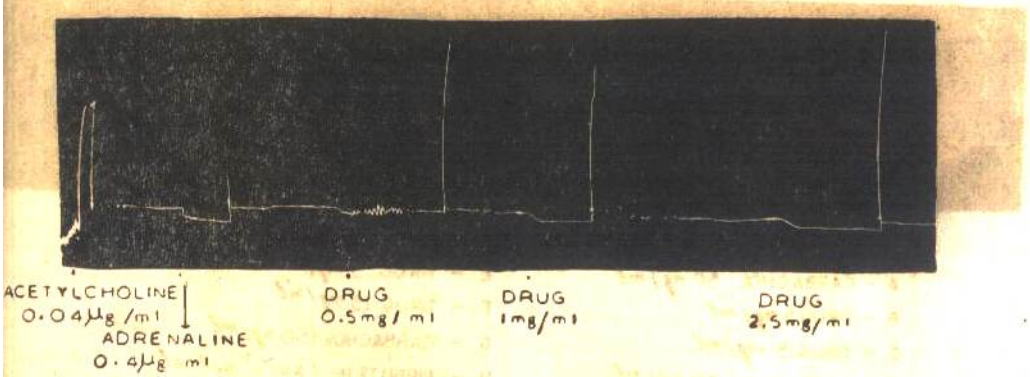


FIG.3

EFFECT OF WATER SOLUBLE FRACTION OF ALCOHOLIC EXTRACT OF DUGDHIKA (E.PROSTRATA) ON HISTAMINE AND ACETYLCHOLINE INDUCED SPASM ON ISOLATED RABBIT ILEUM

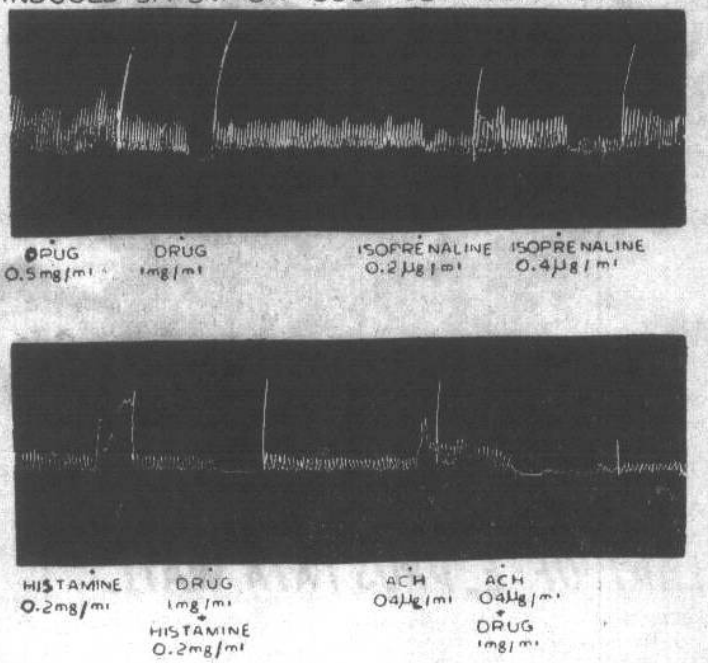
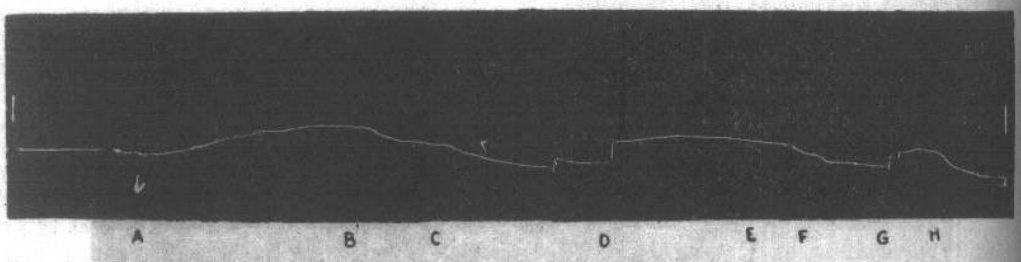


FIG.4

ACTION OF WATER SOLUBLE FRACTION OF ALC. EXT. OF E. PROSTRATA ON CARBACHOL INDUCED SPASM OF GUINEA PIG TRACHEAL CHAIN



A – CARBACHOL 50 ng/ml
B – DRUG 5 mg/ml
C – DRUG 15 mg/ml
D – CARBACHOL 50 ng/ml
E – DRUG 5 mg/ml
F – DRUG 15 mg/ml
G – CARBACHOL 50 ng/ml
H – PIRBUTEROL 2×10^{-5} mol/ml

Discussion

Our observations of the first experiment reveal that the test drug is significantly effective against histamine vapors induced bronchospasm in the dose of 750 mg / kg, intraperitoneally, as the time of developing spasm increased in all the animals of the experimental group while in the control group it remained near about same. On statistical analysis of p-value in the treated group (experimental gr) comes to be <0.01 confirming that the results are significant.

Thus on the basis of the first experiment, it can be inferred that either the test drug (E. prostrata) possess smooth muscle relaxant property by virtue of which the spasm of bronchial muscles is prevented or has anti-histaminic action or both. In order to confirm its mode of action, the drug was studied on the smooth muscles of small intestines of rats and rabbits (Experiment 2 & 3) which showed positive smooth muscle relaxant action as evident from figures 2 & 3. More over, it was also observed that the smooth muscle relaxant action of the test drug could not be blocked wither by alpha (Priscol) or beta (Propanolol) blockers alone or together. Sharma et al (1970) also reported the same findings while using the total alcoholic extract of the mixture of two plants i.e. E. prostrate & E. thymifolia. They were of the view that probably the drug relaxes the smooth muscles directly, similar to aminophylline but not through beta or alpha receptors. However, further studies may reveal its exact mode of smooth muscle relaxation.

The clinical studies conducted by Sharma et al (1981) on the mixture of two plants i.e. E. prostrate & E. thymifolia which proved the same to be beneficial in the treatment of Bronchial asthma, support the present findings and hence there is need to study the presence / absence of smooth muscle relaxant property in E. thymifolia as also in yet another ecotype i.e. green of E. prostrate. If the later species do not possess the anti – asthmatic property a more potent action can be obtained clinically by using only the red ecotype of Euphorbia prostrate.

In our experiments on rabbit intestines, the test drug successfully blocked / prevented the spasmsgenic action of acetyl choline chloride and histamine dihydrochloride as evident from the Figure No.3. If the drug has showed its significant action in our first experiments also due to anti – histaminic action then it should not block the spasmogenic action of acetyl choline.

Therefore, the experiment reveals that either the test drug possesses only non specific direct smooth muscle relaxant activity by virtue of which it prevents the spasmogenic action of all the spasmogens or it has an anti cholinergic and anti histaminic action along with non-specific direct smooth muscle relaxant action which may be considered highly unusual. We therefore, infer from the above study that the test drug relaxes smooth muscles and prevents the spasmogenic action of spasmogens on the smooth muscles of G.I.T..

It is not necessary for a smooth muscle relaxant drug to also have powerful spasmolytic action on bronchial muscles too. Accordingly, the test drug was also studied on carbachol induced spasm of guinea pig tracheal chain. The drug successfully relaxed the spasm of smooth muscles of trachea, clearly indicating that the drug is capable of relaxing the spasm of smooth muscles of trachea and bronchi or in other words it has anti spasmodic action, on tracheo bronchial muscles too and that is

how it relaxes the spasms of bronchial muscles during an asthmatic attack & thus shows beneficial effect in the treatment of bronchial asthma.

CONCLUSION

It can be concluded from the above study that water soluble fraction of total alcoholic extract of Euphorbia prostrate wait (red ecotype) possesses direct smooth muscle relaxant action. The drug probably directly relaxes spasm of bronchial muscles during an asthmatic attack and thus exhibits beneficial effect in the treatment of bronchial asthma. The study paves a path to future workers to isolate and identify the active principle of the plant and to give a new anti asthmatic drug for the service of humanity.

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