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EFFECT OF METHANOLIC EXTRACT OF PHYSALIS ANGULATA ON DIURETIC ACTIVITY

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Abstract

Physalis angulata mainly consists of secosteroids, phenolic compounds, alkaloids, plant steroids and flavonoids. The methanol extract of Physalis angulata was prepared by using Methanol, by maceration method for 72hrs at room temperature against frusemide . The extract was concentrated by simple evaporation at room temperature. A suspension of MEPA in 5% (w/v) Carboxyl Methyl Cellulose (CMC) was prepared for oral administration. As mentioned in table, the diuretic drug like furosemide, and MEPA (250 mg/kg, 500 mg/kg and 1000 mg/kg) of Urine volume were 8.34 ± 0.48, 5.43 ± 0.28, 6.70 ± 0.22 and 7.58 ± 0.62 respectively. Estimation of Na+ (m mol/L) of the diuretic drug like furosemide and MEPA (250 mg/kg, 500 mg/kg and 1000 mg/kg) were 125.62 ± 0.16, 112.46 ± 3.47, 118.24 ± 3.16 and 123.64 ± 3.47 respectively. we can conclude that MEPA treatment produced a marked diuresis when rats were acutely treated. In our study, no lethality was observed at least for the dose and duration used.

Kev words: Physalis angulata, Furosemide, MEPA& Methanol extract

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INTRODUCTION

Roots, plants and minerals were known from ancient to renaissance times to increase the flow of urine, and it was thought that this was helpful in the treatment of cardiac oedema, or dropsy [1]. However, there was no satisfactory treatment for cardiac failure until William Withering discovered the diuretic properties of digitalis in 1775[2]. The era of modern diuretics started with the observation in 1937 that patients receiving the new antibacterial agent sulfanilamide, developed metabolic acidosis and showed an increase in urine p^H [3, 4]. The connection between sulfanilamide and carbonic anhydrase was made in 1940, when the specific inhibition of carbonic anhydrase by sulfanilamide was observed [5, 6].

The enzyme carbonic anhydrase was found in the kidney in 1941 [7]. In 1954 the carbonic anhydrase inhibitor, acetazolamide came on the market. The thiazide diuretic, chlorothiazide was in 1958 released on the market. The increased understanding of the renal handling of sodium in the late 1950's led to the quest for more potent diuretics that could act at a more proximal site of the nephron than thiazides, where larger quantities of sodium are reabsorbed. The search to develop diuretics that are more potent started at two laboratories. One laboratory developed an agent based on the structure of chlorothiazide and eventually synthesized ethacrynic acid, a potent inhibitor of sodium reabsorption in the thick ascending limb of the loop of Henle. The other laboratory took the structure of sulfonamyl derivates as starting point and finally synthesized furosemide in 1959, which was released on the market in 1964 [8-11].

Plant Profile:

Botanical classification:

Kingdom – Plantae
Division - Magnoliophyta
Order - Solanales
Family - Solanaceae
Genus - Physalis L
Species - Physalis angulata L (12).

Synonyms:-

- Physalis capsicifolia
- Physalis lanceifolia
- Physalis ramosissima (13).

DESCRIPTION OF PLANT:

Mullaca is an annual herb indigenous to many parts of the tropics, including the Amazon. It can be found on most continents in the tropics, including Africa, Asia, and the Americas. It grows up to 1 m high, bears small, cream-colored flowers, and produces small, light yellowish-orange, edible fruit sometimes referred to as Cape gooseberry. The fruit is about the size of a cherry tomato, and like tomatoes, it contains many tiny edible seeds inside. Mullaca propagates easily from the many seeds the fruit contains; spontaneous clumps of plants can be found along river banks and just about anywhere the soil is disturbed and the canopy is broken (allowing enough sunlight to promote its rapid growth (13).

Parts used: Whole plant leaves and roots.

Fig 1: Physalis angulata

Chemical Constituents: Physalis angulata mainly consists of secosteroids, phenolic compounds, alkaloids, plant steroids and flavonoids. Some of the constituents established physalins-B, D, F and G, withanolides and secosteroids.

Physalis angulata contain various types of active compounds include saponins, flavonoids,

polyphenols, and physalin, tannin, kriptoxantin, vitamin C, protein, crude fat by the major component of palmitic acid and stearic acid. And the roots contain alkaloids.

Physalins are steroidal constituents of Physalis plants which possess an unusual 13,14-seco-16,24-cyclo-steroidal ring skeleton (where the bond that is normally present between the 13 and 14 positions in other steroids is broken while a new bond between positions 16 and 24 is formed) Since the isolation and the structure determination of Physalin A and Physalin B in 1969, The main plant chemicals isolated in Physalis species: Physalis alkekengi, Physalis angulata, and Physalis lanceifolia, ayanin, chlorogenic acid, choline, ixocarpanolide, myricetin, phygrine, physagulin A thru G, physalin A thru K, physangulide, sitosterol, vamonolide, withaminimin, withangulatin A, withanolide D, withanolide T, and withaphysanolide. These compounds have antimicrobial and antiparasitic effects (14).

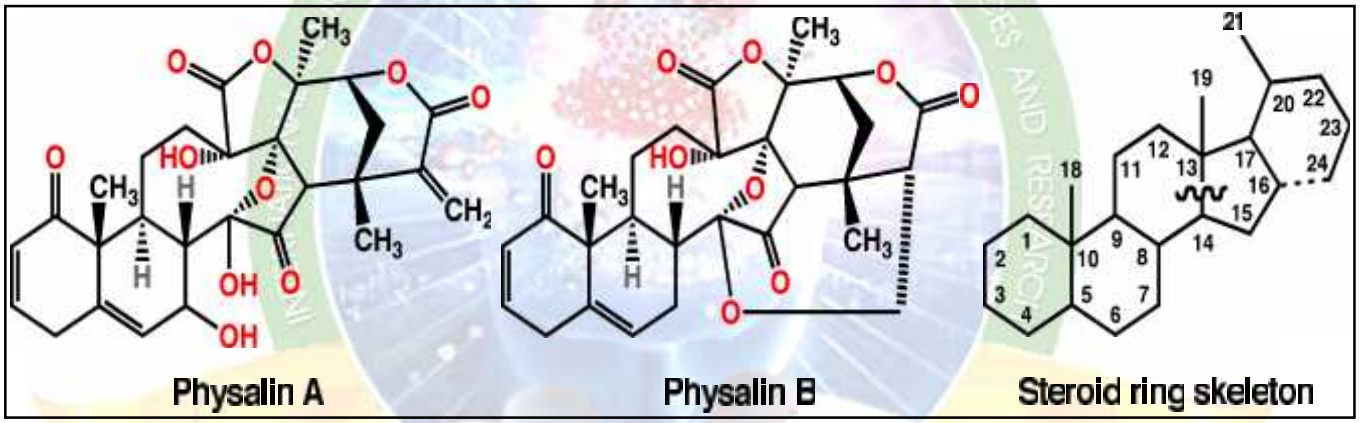

Fig.: Derivatives Physalin Pendula

MATERIALS AND METHODS:-

Experimental Animals and Housing of Animals: Albino Wister rats of both sex (150-250g).The animals were procured from National Institute of Nutrition (Hyderabad) They are maintained under standard conditions (temperature 25 °C) at least 2 weeks prior to the study, so that animals could acclimatize to the new environment. The animals were housed in sanitized polypropylene cages (32x24x16) with stainless steel grill top, bedded with rice husk containing sterile conditions. They had free access to standard pellet diet and water was provided *ad libitum.*

Drugs and Chemicals:-

1. Furosemide inj. (Aventis laboratories limited)

2. Normal Saline.

All Other Chemicals used for this investigation were of analytical grade from S.D, Fine chemicals, Mumbai, India.

Preparation of extract:

The whole plant of Physalis angulata were dried under shade in room temperature for 3 days and powdered and the powder was used for preparation of methanolic extract.

The methanol extract of Physalis angulata was prepared by using Methanol, by maceration method for 72hrs at room temperature. The extract was concentrated by simple evaporation at room temperature. A suspension of MEPA in 5% (w/v) Carboxyl Methyl Cellulose (CMC) was prepared for oral administration.

Selection of dose:

Acute toxicity dose was given in previous literature that is 5000mg/kg. $1/10^{th}$ of dose was considered as therapeutic dose and to identify the dose dependent action the 50% and 200% of therapeutic dose was considered as minimum and maximum dose for further pharmacological evaluation in animal model.

Evaluation of Diuretic activity:

Lipschitz test described by Lipschitz et.al (1943) was employed for assessment of diuretic activity. In this method, albino wistar rats of either sex weight 150 to 200gm were used. The rats were divided five groups of six animals each. The animals were fasted for 24 hours prior to the experiment and water was given ad libitum during fasting.

First group received normal saline (25ml/kg, i.p),

Second group received furosemide (20mg/kg, i.p),

Third, fourth and fifth groups received MEPA (250, 500, 1000mg/kg, p.o.) respectively.

After administration the animals were placed in a metabolic cage (2 per cage), specially designed to separate urine and collected was measured at the end of 5hours. During this period, no food and water was made available to animals. The parameter was taken volume of urine; electrolytes (Na^+, k^+, Cl^-) were estimated in urine for assessment of diuretic activity. The Na^+, k estimated was carried out using flame photometry. The cl^- ion concentration was estimated by titration with 0.02N $AgNo_3$ using 5% potassium chromate solution as indicator.

Statistical Analysis:-

All results are expressed as mean ± standard error. The data was Analyzed using one ways of analysis of variance (ANOVA). The statistical significance of the different of the means was evaluated by Dunnett's test.

RESULTS

The preliminary photochemical test revealed the presence of flavonoid, amino acids, glycosides, and alkaloids in the methanolic extract of *Physalis angulata*.

In the present study revealed that, methanolic extract of *Physalis angulata* significantly, increases the urinary output as well as urinary ion concentration at higher doses.

Table 1: Diuretic Effect of methanolic extracts of *Physalis angulata* in rats.

Treatment	Urine volume (ml/100g/5h)	Na^+ (mmol/L)	K^+ (mmol/L)	Cl^- (mmol/L)
control	4.52 ± 0.58	104.20 ± 1.18	92.18 ± 0.73	58.22 ± 5.18
Furosemide (20mg/kg).	8.34 ± 0.48***	125.62 ± 0.16**	62.04 ± 2.14***	78.24 ± 1.64*
250mg/kg of	5.43 ± 0.28ns	112.46 ± 3.47ns	89.20 ± 2.80ns	55.28 ± 3.18
500mg/kg of MEPA	6.70 ± 0.22*	118.24 ± 3.16**	78.62 ± 1.28***	60.72 ± 5.20
1000mg/kg of MEPA	7.58 ± 0.62***	123.64 ±3.47***	72.40 ± 1.30***	62.46 ± 5.65

Values are expressed as mean±S.E.M; n=6, *P<0.05, **P<0.01, ***P<0.001 considered for significance, (ANOVA followed by Dunnett's test).

As mentioned in table, the diuretic drug like furosemide, and MEPA (250 mg/kg, 500 mg/kg and 1000 mg/kg) of Urine volume were 8.34 ± 0.48, 5.43 ± 0.28, 6.70 ± 0.22 and 7.58 ± 0.62 respectively. Estimation of Na^+ (m mol/L) of the diuretic drug like furosemide and MEPA (250 mg/kg, 500 mg/kg and 1000 mg/kg) were 125.62 ± 0.16, 112.46 ± 3.47, 118.24 ± 3.16 and 123.64 ± 3.47 respectively. Estimation of K^+ (m mol/L) of the diuretic drug like furosemide and MEPA (250 mg/kg, 500 mg/kg and 1000 mg/kg) were 62.04 ± 2.14, 89.20 ± 2.80, 78.62 ± 1.28 and 72.40 ± 1.30 respectively. Estimation of Cl^- (mmol/L) the diuretic drug like furosemide, and MEPA (250 mg/kg, 500 mg/kg and 1000 mg/kg) were 78.24 ± 1.64, 55.28 ± 3.18, 60.72 ± 5.20 and 62.46 ± 5.65 respectively. The methanolic extract was found to produce significant increases in excretion of Na+, K+, Cl- ions at the higher doses tested (1000mg/kg p.o).The order of activity of increases of urinary output was 1000mg >500mg >250mg.The diuretic activity demonstrated by the test extract of 1000mg/kg was significantly lesser than standard drug furosemide (20mg/kg).

DISCUSSION

The diuretic activities of the extracts were significant ($P < 0.05$) when as compared to control. The graded doses of the MEPA in normal saline showed a very significant increase in diuresis, natriuresis, kaliuresis, GFR. All the extracts cause increase urine elimination and increase in Na+, K+ and Cl+ excretion as compared to normal saline. The extracts possibly act by the synergistic action mechanism of the [HCO3 −/Cl−], [HCO3 +/H+] exchangers and the [N+/H+] antiporter, to cause diuresis. There was an increase in the ratio of concentration of excreted sodium and potassium ions after MEPA treatment.

The *Physalis angulata* Extract exerted its diuretic activity possibly by inhibiting tubular reabsorption of water and accompanying anions, as such action has been hypothesized for some other plant species. Therefore *Physalis angulata* extract significantly increased the GFR due to (a) A detergent like interaction with structural components of glomerular membranes. (b) A decrease in renal perfusion pressure, attributable to decrease in the resistance of the afferent arteriole and/or an increase in the resistance of the efferent arteriole and/or. (c) The direct effect on the arteriole wall affecting glomerular blood flow.

As emphasized, diuretic properties of MEPA could be due to other active principles such as flavonoids, glycosides, alkaloids and saponins. It is also possible that diuretic effect of the water MEPA could be due to other secondary active(s) metabolites(s). The other possibility for the observed diuretic effect of MEPA water could be due to indirect changes of some physiological parameters before blood filtration step and/or the consequence of the observed glycosuria.

The observed decrease of urine osmolality could be explained by a marked increase in urinary flow, which seemed to be more important than the possible urinary electrolytes excretion. Administration of the MEPA caused a diuretic response, which was accompanied with a slight increase in GFR. This finding suggests different mechanisms of action, like a direct effect on arterial pressure which could affect GFR or glomerular blood flow by decreasing renal perfusion pressure.

MEPA caused diuresis by a mechanism quantitatively similar to that of furosemide and more than one mechanism seems to be involved. The MEPA did not affect plasma urea levels, urine pH, plasma osmolarity and hematocrite indicating that the rapid physiological regulation of these important parameters was not altered after RR infusion.

CONCLUSION

On basis of the above results, we can conclude that MEPA treatment produced a marked diuresis when rats were acutely treated. In our study, no lethality was observed at least for the dose and duration used. However, advanced toxicological studies remain to be performed in mice and rats. It remains necessary to study eventual adverse effect(s) of this plant such as alteration of some neural, metabolic and hormonal parameters, which are undetermined in this study, before its recommendation to clinical use. The precise site(s) and the molecular and cellular mechanism(s) of MEPA action remain to be elucidated in further studies.

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