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EVALUATION OF ANALGESIC AND ANTI-INFLAMMATORY EFFECT OF TANACETUM PARTHENIUM ON EXPERIMENTAL ANIMALS

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I. INTRODUCTION

It is anticipated that herbal drugs used globally were discovered following leads fromlocal medicine. According to WHO reports that about 25% of modern medicines have been derived from plants which were first used traditionally. Many synthetic analogues are built on models of compounds isolated from plants. Most of the modern medicines in India are derived from natural products. An advanced research effort to describe the advantage of traditional system of medicine with respect to the safety and efficacy could result in a better use of these corresponding systems of medicine which is the need of time to address the issues.

Pain can be defined as, unpleasant sensation, usually evoked by an external or internal noxious stimulus. Analgesic decrease the pain by acting on the CNS or peripheral pain mechanisms, without altering Consciousness So analgesic activity means capacity of a substance to neutralize the pain sensation. The environment has provided a vast collectionof remedies to cure all ailments of

mankind. Since the beginning of human era, along with the food crops, man has cultivated herbs for his medicinal needs. The knowledge of drug has accumulated over thousands of year as a result of mans inquisitive nature, so that today we possess many effective means of ensuring health-care.

Inflammation is the natural response by a living tissue to various kinds of injury. Cyclooxygenase (COX) is the key enzymes in the synthesis of Prostaglandins, Prostacyclin and Thromboxane which are involved in Inflammation, Pain and Platelet Aggregation. 17 Steroidal and non-steroidal anti-inflammatory drugs (SAIDs and NSAIDs, respectively) are currently the most widely used drugs in the treatment of acute inflammatory disorders, though despite their Renal and Gastric negative secondary effects.[6] These drugs block COX-1 and COX-2 enzyme activity. COX enzymes assist with Prostaglandin Production.

NSAIDs, Steroidal Anti-Inflammatory drugs are being used till now, As a result long term uses of these drugs cause adverse side effects and damage human biological system such as liver, gastrointestinal tract, etc on long term use. As a result of adverse side effects can lead to complications, like gastric lesions, cardiovascular, renal failure and gastrointestinal damage in long term.20There is a need for the new safe, potent, nontoxic anti-inflammatory drug. In the present review an attempt has been made to investigate the anti-inflammatroy activity of *Tanacetum partheniu*.

Tanacetum parthenium plant

The perennial plant known as feverfew *(Tanacetum parthenium L.)*, which resembles daisies and is often seen in gardens and by the sides of highways, is a member of the Asteraceae family. The term "fever reducer," febrifugia, is derived from Latin. Feverfew was recommended by the Greek physician Dioscorides in the first century AD for "all hot inflammations." Due to its feathery leaves, it is also known as "featherfew". It is a fragrant, short, bushy perennial that reaches a height of 0.3 to 1 m. Its yellow-green, almost hairless leaves are typically less than 8 centimeters in length and are pinnate to bipinnate (similar to chrysanthemums). Its 2 cm-diameter yellow blooms grow from July to October.

They contain a single layer of white outer-ray florets and resemble those of chamomile (Matricaria chamomilla), with which they are occasionally mistaken. The powerful, harsh scent emanates from this fragrant shrub. It's the alternating, downward-facing yellow-green leaves have small hairs and grow at different levels on both sides of the stem. The tiny yellow

blooms resemble daisies and are grouped in a thick, flat-topped cluster.

Figure 1: ***Tanacetum parthenium plant.***

Chemistry of *tanacetum parthenium*

Feverfew's chemistry is now fully understood. Parthenolide is the primary sesquiterpene lactone, which is the most significant physiologically active component. Parthenolide makes up up to 85% of the total sesquiterpene content and is detected in the superficial leaf glands (0.2%–0.5%) but not in the stems.

II. MATERIALS AND METHODS

Plant collection

Tanacetum parthenium plant was purchased from local market, Raipur Chhattisgarh.

Drying and Pulverization of the plant material

Plant were shade dried and pulverized and passed through 20 mesh sieves.

Preparation of the plant extract

Plant material was extracted through cold maceration process by using mixture of alcohol 8:2 ratio. After keeping in orbital shaker for 24 hour it was filtered solvent was removed by using vacuum evaporator. The resulting ethanolic extract of the *Tanacetum parthenium* was subjected to phytochemical study.

Phytochemical analysis

The ethanolic extract of *Tanacetum parthenium.* Were subjected to qualitative phytochemical tests for different constituents such as alkaloids, carbohydrates, glycosides, flavonoids, phenolic compounds, proteins, and free amino acids and triterpenoids.

1. Test for carbohydrate

Small quantity of extract was dissolved in 5ml of water and filtered.

Molisch test

The filtrate was treated with a few drops of α- napthol (20% in ethyl alcohol). Then 1 ml of concentrated H_2SO_4 was added along the sides of inclined test tube and observed for formation of violet coloured ring at the interface.

2. Test for glycosides and anthroquinones

Borntrager's test

A small amount of ethanolic extract was hydrolysed with hydrochloric acid for few hours on water bath and the hydrosylate was extracted with benzene. The benzene layer was treated with dilute ammonia solution and observed for the formation of reddish pink colour.

Legal test

The extract was dissolved in pyridine and made alkaline with few drops of 10% NaOH and freshly prepared sodium nitroprusside was added and observed for formation of blue colour.

3 Test for flavonoids

Ammonia test

Filter paper strips were dipped in the dilute solution of the extract, ammoniated andobserved for colour change from white to yellow.

4. Test for Tannins and Phenolic compounds

The extract was dissolved in distilled water and dissolved into three portions. Sodium chloride (10%) was added to one portion, 1% gelatine to second portion and gelatine salt reagent to third portion. Precipitation with later or both gelatin salt reagents was indicative of the presence of tannins. Precipitation with salt solution indicates a false positive test. Positive tests were further confirmed by the addition of a few drops of diluteferric chloride (1%$FeCl_3$) to the test extract which gave blue or green black coloration.

5. Test for Proteins and Amino acids

Small amount of extract was dissolved in distilled water and filtered.

Biuret's test

To the ammoniated alkaline filtrate add 2-3 drops of 0.002% copper sulphate andobserved

for appearance of red or violet colour.

Millon's test

To 2 ml of filtrate 5-6 drops of millons reagent (1 g of mercury + 9 ml of fuming nitric acid solution) was added and observed for red precipitates.

Ninhydrin test

To the filtrate lead acetate solution was added to precipitate tannins and filtered. The filtrate was spotted on paper chromatogram and sprayed with ninhydrin reagent and heated at 110ºC for five minutes and observed for red or violet colour.

Xanthoprotein test

To the filtrate a few drops concentrated nitric acid was added by the side of test tube and observed for appearance of yellow colour.

6. Test for Sterols and Triterpenes

The extract was refluxed with alcoholic potassium hydroxide until the completion of saponification. Then the mixture was diluted with distilled water and extracted with diethyl ether. The ethereal extract was evaporated and the unsaponifiable matter was subjected to the following tests.

Libermann - Buchard's test

The ether soluble residue was dissolved in chloroform and a few drops of acetic anhydride was added followed by a few drops concentrated sulphuric acid form sides of the test tube and observed for the formation of blue to blue- red colour.

Salkowski's reaction

To the ether soluble residue 2 ml of concentrated sulphuric acid was added and observed for the formation of yellow ring at the junction which turns red after one minute.

- **Animal**

Experimental animals were supplied by Columbia Institute of Pharmacy, Raipur, Chhattisgarh. Wistar albino rats (150-200 g) were placed in polypropylene cages at temp. (25±2°C) and (50±5%) RH, under 12/12 light/dark cycle. Animals were provided with Rodent pellet diet supplied by Kevel sales, was provided and water *ad libitum*. Experimental protocol was approved by IAEC, Columbia institute of Pharmacy. approval number:

CIP/IAEC/2022/191.

III. Pharmacological studiesanalgesic activity

- **Hot plate method**

The hot plate assay method was employed for the purpose of preferential assessment of possible centrally medicated analgesic effects of ethanolic extract of *Tanacetum parthenium.* Diclofenac was used for positive control group. In this experiment, four groups (n=5) of Swiss albino rats (150-200 gm). Food was withdrawn on the preceding night of the experiment. Group I- Normal Control received CMC (0.5%), and Group II- standard treated with Diclofenac (3 mg/kg i.p), whereas group III and IV- animals were treated orally with hydroalcoholic extract of *Tanacetum parthenium* (100 and 200 mg/kg respectively).[41] Each animal was then individually placed gently on Eddy's hot plate at 55ºC. Latency to exhibit nociceptive responses such as licking paws or jumping off the hot plate were determined at 30, 60, 90 and 120 min after administration of the drugs or vehicle.

- **Tail immersion test[43]**

This method assessment was used to evaluate the analgesic effects of hydroalcoholic extract of *Tanacetum parthenium.* The wistar rats were divided into four groups each consists of six animals. They were placed into individual restraining cages leaving the tail hanging out freely. The lower 5cm portion of the tail is marked and this part of the tail was immersed in a water bath containing water at a temperature of 55± 0.5 ºC. Withdrawing the tail from the hot water showed the analgesic effect. The reaction time was noted on a stop-watch. Each animal served as control. The average of the two values was the initial reaction time.

Group I- Normal Control received CMC (0.5%), and Group II- standard treated with Diclofenac (3 mg/kg i.p), whereas Group III and IV- animals were treated orally with hydroalcoholic extract of *Tanacetum parthenium* (100 and 200 mg/kg respectively).The reaction time of the groups were taken at 0, 30, 60, 90 and 120min. The cut off time ofthe immersion was 15seconds. The reaction time was measured.

- **Anti-inflammatory activity**

Carrageenan-induced paw edema in rats

For this experiment, the rats (120-150g) were divided into four groups (n=5). Group I- Normal Control received CMC (0.5%), and Group II- standard treated with Diclofenac (3 mg/kg i.p), whereas group III and IV- animals were treated orally with hydroalcoholic extract of *Tanacetum parthenium* (100 and 200 mg/kg respectively). Acute inflammation was

produced by injecting 0.1 ml of 1% (w/v) carrageenan suspension into the sub planterregion of the right hind paw of the rats. The animals were pretreated with the drug 1hour before the administration of carrageenan. The paw thickness was measured at 1, 2, 3 and 4 h after carrageenan injection by using digital vernier calipers.

IV. RESULTS

1. Phytocjemical evaluation of *tanacetum parthenium*

Table 1: Qualitative phytochemical evaluation.

Parameters	Hydro alcoholic extract
Alkaloid	-
Carbohydrates	+
Flavonoids	+
Tannins & Phenolic compounds	+
Proteins & Amino acids	+
Saponins	-
Sterols or Triterpenes	+

2. Pharmacological studiesanalgesic activity

Table: 2 Anti-inflammatory effects of hydroalcoholic extract of TPM in Wister albino rats.

Group	Base line	60 min	2 hr	3hr
Control (Saline)	1.46±0.05	1.46±0.05	1.46±0.05	1.46±0.05
Standard (Diclofenac)	1.46±0.04	1.5±0.07*	1.9±0.02*	2.4±0.07*
TPM 100 mg/kg	1.6±0.05	1.8±0.05*	2.36±0.12*	2.58±0.12*
TPM 200 mg/kg	1.6±0.05	1.74±0.07*	2.28±0.18*	2.42±0.09*

Values were Mean ± SEM,(n=5), *P<0.05 Vs control. Data were analyzed byusing One-way ANOVA followed by Dunnett's test.

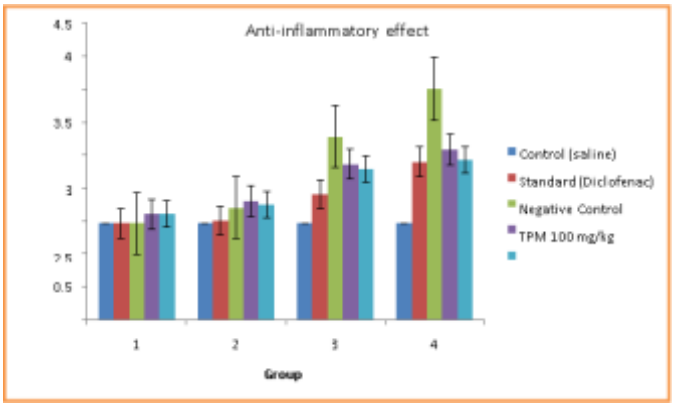

Figure 2: Anti-inflammatory effect of hydroalcoholic extract of TPM in wister albino rats.

Table 3: Tail withdrawal reflex effect of hydroalcoholic extract of TPM in wisteralbino rats.

Group	Before treatment	After treatment	Difference	
	Mean± SEM	Mean± SEM	Mean± SEM	% Inhibition
Control (Saline)	1.31 ±0.02	1.31±0.02	0	0
Standard (Diclo)	1.37± 0.08	3.65± 0.2*	2.28±0.24	61.88
TPM 100 mg/kg	1.52±0.04	2.4±0.07*	0.88±0.08	36.45
TPM 200 mg/kg	1.32±0.02	3.64±0.05*	2.32±0.06	63.58

Values were Mean ± SEM, (n=5), *P*<0.05 Vs control. Data were analyzed byUsing One-way ANOVA followed by Dunnett's test.

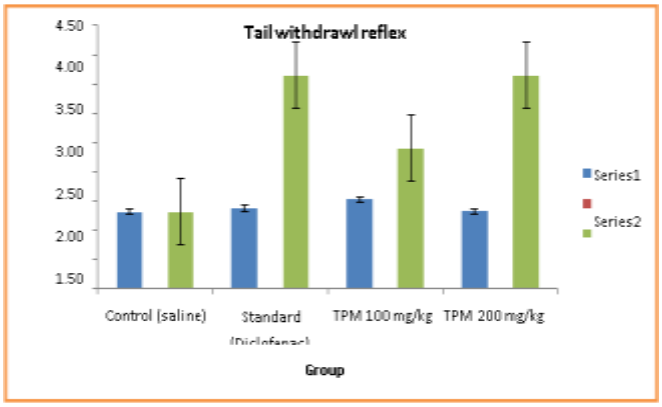

Figure 3: Tail withdrawal reflex effect of hydroalcoholic extract of TPM in wister albino rats.

Values were Mean ± SEM,(n=5), *P*<0.05 Vs control. Data were analyzed byUsing One-way ANOVA followed by Dunnett's t

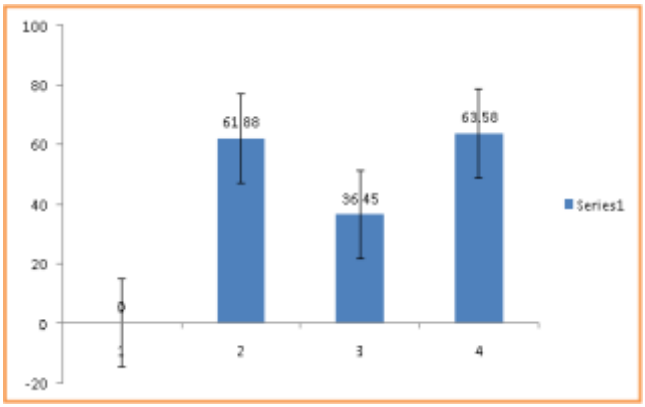

Figure 4: Percentage inhibition of tail withdrawal reflex.

Table 4: Analgesic effect of hydroalcoholic extract of TPM on hot plate test in wistar albino rats.

Group	Base line	60 min	2 hr	3 hr
Normal Control (Saline)	0.238±0.01	0.46±0.03	0.512±0.02	0.52±0.004
Standard (Diclofenac)	4.01±0.12	9.52±0.34*	7.3±0.13*	6.52±0.07*

TPM 100 mg/kg	2.3±0.17	4.9±0.18*	3.8±0.19*	3.38±0.16*
TPM 200 mg/kg	3.1±0.13	6±0.2*	4.12±0.18*	4.12±0.1*

Values were Mean ± SEM,(n=5), *P*<0.05 Vs control. Data were analyzed byUsing One-way ANOVA followed by Dunnett's test

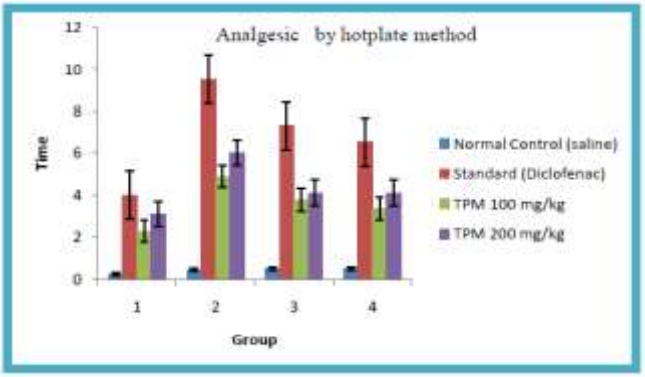

Figure 5: Analgesic effect of hydroalcoholic extract of TPM on hot plate test in wistar albino rats.

V. CONCLUSION

The present thesis entitled "Evaluation of Analgesic Anti-Inflammatory Effect of *Tanacetum Parthenium* on Experimental Animals*."* deals with the exploration of pharmacological and phytochemical screening of the selected Indian medicinal plant*Tanacetum Parthenium*. The results obtained from the preliminary phytochemical screening of *Tanacetum Parthenium* extract showed the presence of flavonoids, alkaloids, tannins as shown in Table 1. It was reported that the flavonoids frequently found in plantsposses analgesic, antipyretic and anti-inflammatory activity.

It was pulverized and extracted with ethanol using soxlet apparatus. The resulting extract was concentrated. The study of the plant *Tanacetum Parthenium* was done by using rats with the oral doses of 100, & 200 mg/kg body weight. As for the analgesic effect, the leaf extract appear to act via the central and peripheral mechanisms of analgesia by using hot plate, tail immersion and finally anti-inflammatory effect of plant extract was done by using carrageenan- induced paw edema in rats.

The *Tanacetum Parthenium* has shown a significant anti-inflammatory and analgesic effects. These effects maybe because of the presence of phytochemicals such as flavonoids, tannins and terpenoids present in the plant extract The Present study showed that the ethanolic leaves extract *of Tanacetum Parthenium*, posses peripheral and central analgesic activity in animal

model. *Tanacetum Parthenium* showed anti-inflammatory activity in different animal model. Flavonoids and tannins are the major constituents of *Tanacetum Parthenium* leaves, which may be responsible for its Analgesic and Anti- inflammatory activity. Further detailed study on *Tanacetum Parthenium plant* using different flogestic agents in this area will enable us to understand the mechanism of actionunderline the above mention activity.

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