EVALUATION OF ANALGESIC ACTIVITY OF NSAID IN CHOCOLATE DOSAGE FORM

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Abstract: Current study was undertaken to investigate the release of the drug and analgesic activity of orally administered Diclofenac sodium chocolate dosage form by using tail flick and hot plate method in rat model. In these methods, heat is the source for pain. The time course for analgesia revealed maximum activity after 3 hours in both tail flick and hot plate methods. A constant heat (55°C) will be given to the animal by both hot plate and tail flick methods and the response of animals e.g. jumping, paw licking and withdrawal will be observed. The Diclofenac Sodium used for the analgesic activity (10mg/kg) was formulated as chocolate formulation and given orally. Both the test and standard drugs reduced the pain significantly as compare to the control group. The results of pharmacological tests performed in the present studies suggest that the drug is being release from the formulated dosage form and possess potent analgesic activity.

Index terms: **Analgesic activity, chocolate dosage form, diclofenac sodium, hot plate method.**

I. INTRODUCTION

Diclofenac Sodium chemically, 2-(2-(2,6-dichlorophenylamino)phenyl) acetic acid. Diclofenac Sodium sold under the trade names Voltaren among others, is a non steroidal anti-inflammatory drug used to treat pain and inflammatory diseases such as gout. It is taken by mouth or applied to skin. Improvements in pain typically occur with in half an hour and last for as much as 8hr. The anti-inflammatory effects of Diclofenac are believed to be due to inhibition of both leukocyte migration and the enzyme cyclooxygenase (COX-1 and COX-2), leading to the peripheral inhibition of prostaglandin synthesis. As prostaglandins sensitize pain receptors, inhibition of their synthesis is responsible for the analgesic effects of Diclofenac.

Pain is the most common clinical complaint and causes considerably human suffering. In the US alone, approximately 100 million people suffering from moderate pain during any given year. NSAIDS are most commonly prescribed drugs for acute and chronic pain. Developing an ideal pain model to evaluate analgesic in healthy human volunteers is difficult. World Health Organization (WHO) has suggested a pain management protocol which states that simple analgesic should be selected first and in case the patient does not respond to that, one can choose any other NSAID and thereafter give a combination of NSAID with Opioid analgesic.

Now a days, every prescription consists of various categories of drugs which need to be administered at regular intervals mostly by oral route. This kind of frequent oral administration of various drugs makes the patient uncomfortable due to difficulty in swallowing. A part from the dosage form, organoleptic properties of the drug need to be given is a serious thought during the manufacturing process. Improved patient compliance can be obtained by delivering active pharmaceutical ingredient in an attractive form which results in reduced rejection / psychological inhibition towards dosage forms. Keeping this in view a new attractive and highly acceptable form of formulation is developed.

The present study was therefore undertaken to investigate the release of Diclofenac Sodium from chocolate formulation and analgesic activity of drug when formulated as chocolate dosage form with the aim of developing a new formulation with the pharmacological basis for its use to treat pain.

II.MATERIALS AND METHODS

For knowing the release of a drug from a chocolate dosage form diclofenac sodium was selected and obtained as a gift sample from Hetero drugs, Hyderabad. Chocolate dosage form of the drug for the study was prepared in the laboratory. All the procedures carried out in the study were approved by Institutional Animal Ethical Committee (IAEC) of A.M. Reddy Memorial College of Pharmacy, Narasaraopet.

2.1 Preparation of standard solution

Diclofenac sodium (10mg/kg body weight) was dissolved in sufficient quantity of distilled water. It was then transferred to 100ml volumetric flask and dissolved initially by using 30ml of distilled water and finally made to final volume.

2.2 Preparation of sample solution

Diclofenac sodium chocolate dosage form was taken and crushed using mortar and pestle, accurately weigh formulated dosage form containing (10mg/kg) was dissolved in sufficient quantity of distilled water. It was then transferred to 100ml volumetric flask and dissolved initially by using 30ml of distilled water and finally made to final volume.

2.3 Selection of experimental animals

Healthy albino rats of either sex weighing 175-275g were used in this study. The animals were housed comfortably in a group of three in a single clean plastic cage with a metal frame lid on its top. They were housed under standard environmental conditions of temperature (24±1°c) and relative humidity of 30-70%. A 12:12h light dark cycle was followed. All animals had free access to water and standard pelletized laboratory animal diet and libitum.

III. EVALUATION OF ANALGESIC ACTIVITY

Albino rats weighing 175 grams to 275gm were divided into three groups and six in each group with individual marking. Animals were unfed 12hours prior to drug administration till completion of the study. The test and standards were given orally in both the methods.

Group -1: Normal saline will be supplied and served as control.

Group -2: Animals received a dose of 10mg/kg of diclofenac sodium IP and served as standard.

Group -3: Animals received 10mg/kg of diclofenac sodium chocolate and is test.

3.1 Hot plate method

The temperature is controlled for 55±1°C. The animals were placed in hot plate on heated surface on the time (sec) to discomfort reaction (jumping, withdrawal) was recorded as response period to 0, 1, 2, 3 and 4 hours following oral administration of test and standard compounds. A latency period of 15 min was identified as complete analgesia and the measured was terminated if it exceeded the latency period in order to avoid injuring.

3.2 Tail flick method

The method was carried out using analgesiometer. Tail flick method measures the time taken to withdraw tail from the thermal source recorded as reaction time and opioid like analgesics increase threshold time of such Tail flicking. The tail flick latency was obtained thrice before drug administration and mean used as per drug latency. The tail flick latencies were measured at 0, 0.5, 1, 2, 3 and 4 h after the administration of drug. A cut off time of 10sec was planned to avoid any tissue damage in the animal. Results of tail flick latencies were expressed in terms of reaction time in seconds.

IV.RESULTS AND DISCUSSIONS

Hot plate and Tail flick methods are the most common test for evaluating the analgesic efficacy of drugs. The standard diclofenac sodium and the chocolate formulation given orally elicited a significant analgesic activity in both methods as by increase in latency time in seconds as compared with vehicle control. The reaction times of the standard and test by hot plate method and tail flick method were tabled in Table 1 and Table 2 respectively. All the values for both methods are mean±SEM. Graphical representation of the reaction times with respect to time interval is shown in Fig. 1 and 2 for hot plate method and tail flick method respectively.

Table 1: Analgesic activity by Hot plate method in rats

Group Treatment	Reaction time(sec)					
	0 min	0.5 h	1h	2h	3h	4h
Normal Saline (Control)	2.13±0.129	1.75±0.183	2.90±0.168	3.27±0.135	4.90±0.241	4.52±0.153
Diclofenac sodium (10mg per kg)	3.14±0.311	5.50±0.342	7.12±0.273	10.43±0.232	14.12±0.133	12.54±0.264
Diclofenac sodium chocolate (10 mg / kg)	2.97±0.147	5.43±0.228	6.96±0.312	9.16±0.263	13.96±0.212	11.91±0.151

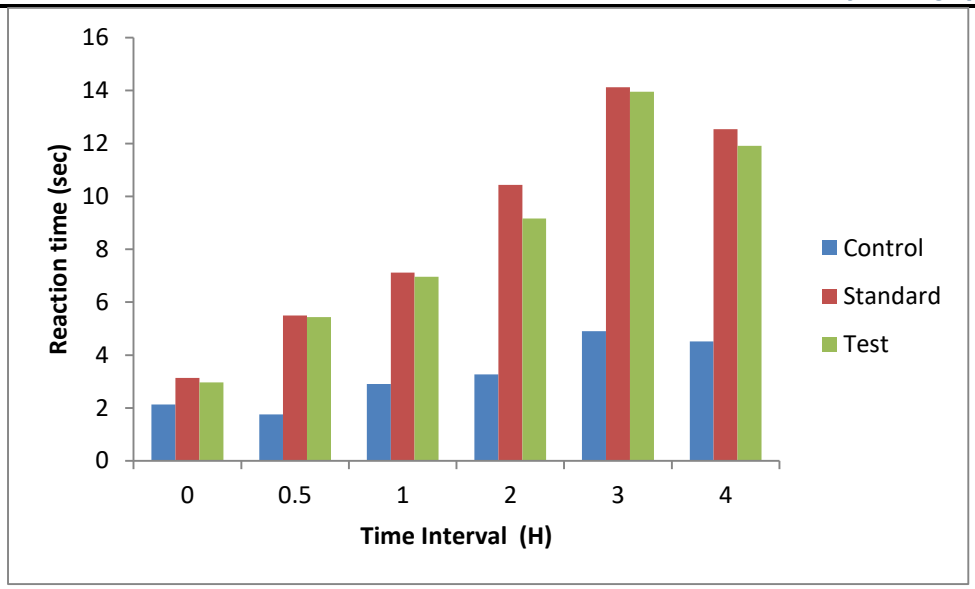

Figure 1: Analgesic activity by hot plate method in rats.

Table 2: Analgesic activity by Tail Flick method in rats

Group Treatment	Reaction time (sec)					
	0 min	0.5 h	1h	2h	3h	4h
Normal saline (Control)	2.43±0.082	2.51±0.037	3.15±0.142	3.04±0.028	3.08±0.072	2.96±0.054
Diclofenac sodium (10 mg / kg)	2.24±0.061	3.62±0.092	4.53±0.175	6.01±0.033	9.41±0.081	7.51±0.281
Diclofenac sodium chocolate (10 mg / kg)	2.03±0.18	3.35±0.282	4.64±0.251	5.85±0.025	9.12±0.091	6.84±0.172

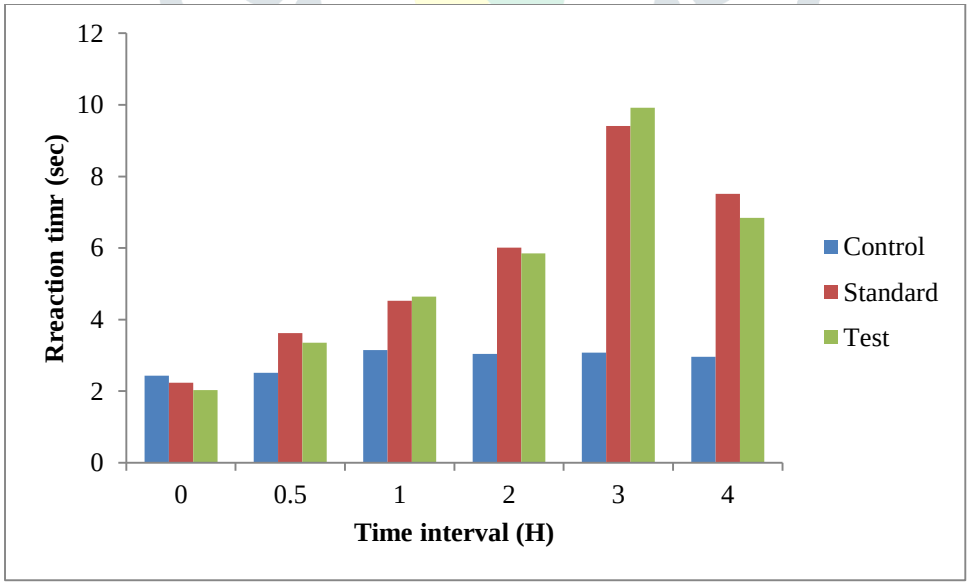

Figure 1: Analgesic activity by tail flick method in rats

Results of hot plate method and tail flick method showed significant reduction in pain at 3hours following standard and test when as compared to control. Increase in mean reaction time by diclofenac in the standard group was significantly higher which is 14.12±0.133 in hot plate method and 9.41±0.081 in tail flick method than test which showed the mean reaction time at 13.96±0.212 and 9.12±0.091 when compared to control at 4.90±0.241 and 3.08±0.072 in hot plate method and tail flick method respectively.

With the aim of bringing out an effective and attractive palatable dosage form, diclofenac sodium was incorporated into chocolate formulation. The release of drug from the formulation and its potential to show the analgesic activity as chocolate formulation was investigated by comparing the formulation with the standard diclofenac sodium drug. Hot plate method and tail flick method were found to be suitable for the study.

The present experimental evaluation revealed that the diclofenac is being released from the chocolate formulation and is exhibiting significant analgesic activity similar to that of standard drug when compared to control in rats and the maximum activity is seen at 3hour of the time interval.

V. CONCLUSION

In conclusion, the study demonstrated that the diclofenac sodium chocolate has a significant analgesic activity as that of diclofenac sodium drug. Drugs can be formulated as an effective and palatable dosage forms without any change in their pharmacological action. Further studies will be necessary to prove the safety and efficacy of long term administration of the chocolate formulation.

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