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A COMPARATIVE STUDY OF ANALGESIC AND ANTI-INFLAMMATORY ACTIVITIES OF DICLOFENAC SODIUM IN SOME GENERIC AND BRANDED DRUGS

Suranjan Bantupalli [1], Atluri Deekshit [1], Bala Yaswanth S. Kumar [1], Radha B. Madhavi [2] and Kanaka Durga Devi Nelluri [*1]

KVSR Siddhartha College of Pharmaceutical Sciences [1], Vijayawada - 520008, Andhra Pradesh, India.
Shri Vishnu College of Pharmacy [2], Vishnupur, Bhimavaram - 534202, Andhra Pradesh, India.

Keywords:

Anti-inflammatory effect, Analgesics effect, Eddy's hot plate method, Pletheysmometer

Correspondence to Author:
Dr. Nelluri Kanaka Durga Devi

KVSR Siddhartha College of Pharmaceutical Sciences, Vijayawada - 520008, Andhra Pradesh, India.

E-mail: nelluriss@rediffmail.com

ABSTRACT: Pain is the most common symptom of disease, which accompanies us from an early age. It is a safeguarding mechanism of the body from harmful stimuli. The definition of pain states that it is a subjective sensory and emotional experience. This study compared generic and brand drugs' analgesics and anti-inflammatory activity using eddy's hot plate method and plethysmometer models. Two studies were conducted by using oral and intraperitoneal routes of administration. In this study, generic drugs such as Ranbaxy, intagesic, and Diclovin. Branded drugs are such as Voveran, Dynapar, and Cipla are used. The analgesics activity and anti-inflammatory activity of generic and branded drugs are the same. So, it has been concluded that generic drugs also show same effect as branded drugs.

INTRODUCTION: Pain is as an unpleasant sensory as well as an emotional experience that is associated with potential tissue damage [1, 2]. Based on the main characteristics like symptoms, mechanisms, and syndromes, pain is classified as nociceptive pain, neuropathic pain and inflammatory pain [3, 4]. NSAIDs are the commonly prescribed drugs for treatment of mild to moderate pain and inflammation. They are used in acute conditions like fever, headache and chronic conditions like rheumatoid arthritis, osteoarthritis, *etc*. Diclofenac sodium is one of the most widely used drug among NSAIDs that act by inhibiting the cyclo-oxygenase (COX) enzymes which are responsible for the prostaglandins production [5, 6]. Branded drugs are the medicines that a company names for advertising that drug. Generic names are International Non-proprietary Name (INN). Branded medicines are the original medicines developed by a company, and several companies may manufacture the same generic drug, to which each company can give its own brand name [7, 8].

The generic drug is a product similar to a brand or innovator drug in dosage form, strength, route of administration, quality, characteristics, and intended use. It should contain the same active ingredients as the original formulation; however, the excipients (inactive ingredients) may differ, and the product may also be slightly different in organoleptic properties. The main difference is cost. Generic medicines are usually less expensive than the branded drugs. There is usually competition among generic drug manufacturers. The present research aimed to perform pharmacodynamic studies and compare the

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pharmacological effect between selected generic products and branded generic products of diclofenac sodium [9, 10].

MATERIALS AND METHODS [11, 12]: The analgesic activity was tested by two methods and by both intraperitoneal route and the oral route of drug administration.

Analgesic Activity by Using Hot Plate Method

Materials: Measuring cylinder, Weighing machine, 5 ml injection, 1 ml injection, Saline solution, distilled water.

Animals: Albino Wistar Rats

Apparatus: Eddy's Hot Plate

Principle: Diclofenac was taken as an example of an anti-inflammatory drug. In the hot plate method, we used heat as the main stimulus or source of pain. Mice are the choice of animal for this experiment. The plate in this device gets heated by the heating coil present inside. The animals are placed on the hot plate one by one. The temperature of this device is kept constant at 55 ºC. Licking the paw and jumping reaction of the animal are recorded as the endpoint of the experiment. Analgesic activity increased the reaction time.

Procedure:

- Firstly all the rats were weighed and numbered them accordingly on their tail. (at the base)
- Basal reaction time was noted when rats started licking their paw or started jumping, which appeared first. The normal response time is around- 7-9 sec. The animals that are not responded up to 15 sec were removed from the experiment.
- Diclofenac was injected by the subcutaneous route, and the reaction time was noted at - 15, 30, 60 and 120 min after the morphine injection. After the administration of the drug the reaction time increased was noted as the max time for response.
- Percent increase of the response time was calculated based on response time before and after administration of the drug.

- Anti -Inflammatory activity by using Plethysmometer

Materials: Diclofenac, Carrageenan by preparing 1% w/v solution and by injecting its 0.1 ml to the plantar region of rat

Animals: Rat (150-200 g)

Equipment: Plethysmometer.

Principle: Diclofenac was selected as an anti-inflammatory drug. Carrageen was used as a stimulus or agent which causes inflammation. Cargeenanis a sulphated polysaccharide obtained from seaweed that causes Oedema- Pus with inflamed tissue. Whenever any antigen enters into the body, our body's protective mechanism (Antibody) starts protecting us and the inflammation is the response to that event.

We can say that is part of the host defense mechanism. Several tissue factors play an active and important role in the mechanism of inflammation. These include- release of histamine, bradykinin, and prostaglandins. Inflammation shows the following characteristic sign- Heat-Pain-Redness- Swelling. The agent which gives relief from inflammation is called an anti-inflammatory drug. They work by inhibiting the release of histamine and blocking the conversion of Prostaglandin into COX, Especially COX-II.

The rat's inflammatory reaction is rapidly produced in the form of paw edema by utilizing the stimulus or irritating agent like carrageenan, formalin solution, bradykinin, histamine, mustered, or egg white. When these agents are given an injection in the rat paw, sudden swelling occurs because histamine, 5HT, bradykinin, and prostaglandins release.

Procedure:

- The rats were weighed and numbered them accordingly on their tail. (At the base)
- A mark is made on both the hind paw of the experimental rat, from 2 cm above the paw. It's done just to ensure the proper and same dipping of paw each time.

- Note down the initial paw volume of left and right paw of rat just by observing the level of displaced mercury.
- The animals were divided into two groups having minimum 0.4 rats. In one group, simple saline was injected and, in another group, the drug of study, diclofenac, was injected.
- After 30 min. 0.1 ml of carrageenan was injected into the left paw of rat and it was
- Treated as a control group.
- The right paw was kept as it is and wastreated AS reference for non-inflamed paw for comparison.
- The paw volume of both legs of control and diclofenac treated rats was noted at 15, 30, 60 and 120 min.
- The % difference in both paws of rat of control and diclofenac treated group was calculated as per the reduction of edema.

TABLE 1: DETAILS OF THE FORMULATIONS

S. no.	Drug	Manufactured by	Mfg Lic No	Batch no	Mfg Dt	Exp Dt
1	Ranbaxy (Branded)	Ranbaxy Laboratories Ltd, Mumbai, India	MNB/07/558	F/F/001-A	May 2019	April 2022
2	Intagesic (Generic)	Int as pharmaceuticals Ltd, Gujarat, India.	5/UA/2017	T-111108	July 2018	June 2021
3	Dynapar (Branded)	Troikaa Pharmaceuticals Ltd, Gujarat, India.	DD/L/787	F.DAD.SN.0.06	Jan 2020	Feb 2022
4	Voviran (Generic)	Novartis India Ltd, Mumbai, India.	S-MB/13/136	AT10920	May 2019	April 2022
5	Cipla (Branded)	Cipla house, Mumbai, India.	M.L.74/UA/LL/2007	083HM	July 2018	June 2021
6	Dicoliv(Generic)	Ind swift laboratories Ltd, Chandigarh, India,	78/UAI/2016	TIS-17386	July 2020	June 2021

RESULTS:

Evaluation of Analgesic Activity by Intra Peritoneal Route of Administration:

TABLE 2: RANBAXY BRANDED DRUG, DOSE: 45mg TABLET BY INTRAPERITONEAL ROUTE USING HOT PLATE METHOD IN RATS

S. no.	Body Weight	Dose (mg)	Dose (ml)	0 min (sec)	30 min (sec)	1 h (sec)	2 h (sec)	3 h (sec)	4 h (sec)
1	200g	2mg	0.8ml	8	9	11	13	10	8
2	220g	2.2mg	0.88ml	6	7	9	11	9	6
3	240g	2.4mg	0.96ml	6	8	9	11	10	6
4	240g	2.4mg	0.96ml	6	7	9	10	8	6
5	220g	2.2mg	0.88ml	6	7	9	11	8	6
6	210g	2.1mg	o.84ml	6	8	9	11	9	7

TABLE 3: INTAGESIC GENERIC DRUG, DOSE: 75mg AM PULE BY INTRAPERITONEAL ROUTE USING HOT PLATE METHOD IN RATS

S. no.	Body Weight	Dose (mg)	Dose (ml)	0 min (sec)	30 min (sec)	1 h (sec)	2 h (sec)	3 h (sec)	4 h (sec)
1	280g	2.8mg	0.37ml	7	8	9	11	9	7
2	280g	2.8mg	0.37ml	5	7	8	11	9	5
3	280g	2.8mg	0.37ml	8	9	9	12	9	8
4	280g	2.8mg	0.37ml	8	9	9	12	10	8
5	280g	2.8mg	0.37ml	5	7	8	10	7	5
6	280g	2.8mg	0.37ml	7	8	9	11	9	7

The Hot plate method is useful in elucidating centrally mediated ant nociceptive responses, which focuses mainly on changes above the spinal cord level.

The generic drug (INTAGESIC) significantly ($p<0.05$) reduced the pain as compared to the branded drug (RANBAXY) when administered by the intraperitoneal route.

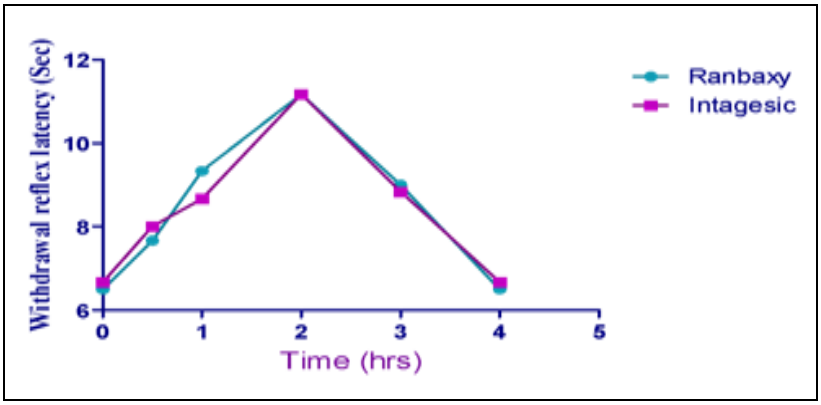

FIG. 1: COMPARISON OF RANBAXY AND INTAGESICDRUGS FOR ANALGESIC ACTIVITY BY INTRAPERITONEAL ROUTE OF ADMINISTRATION USING HOT PLATE METHOD IN RATS USING STUDENT T-TEST AT P<0.05.

TABLE 4: DYNAPAR BRANDED DRUG, DOSE: 75mg AMPULE BY INTRAPERITONEAL ROUTE USING HOT PLATE METHOD IN RATS

S. no.	Body Weight	Dose (mg)	Dose (ml)	0 min (sec)	30 min (sec)	1 h (sec)	2 h (sec)	3 h (sec)	4 h (sec)
1	300g	3mg	0.4ml	9	10	13	15	9	5
2	300g	3mg	0.4ml	5	7	8	12	7	5
3	320g	3.2mg	0.42ml	5	8	8	11	7	5
4	290g	2.9mg	0.38ml	5	7	8	11	7	5
6	300g	3mg	0.4ml		8	8	12	8	6
8	310g	3.1mg	0.41ml		9	10	12	7	8

TABLE 5: VOVIRANGENERIC DRUG, DOSE: 75mg AM PULE BY INTRAPERITONEAL ROUTE USING HOT PLATE METHOD IN RATS

S. no.	Body Weight	Dose (mg)	Dose (ml)	0 min (sec)	30 min (sec)	1 hr (sec)	2 hrs (sec)	3 hrs (sec)	4 hrs (sec)
1	280g	2.8mg	0.37ml	5	6	8	11	7	5
2	290g	2.9mg	0.38ml	5	7	8	12	8	5
3	280g	2.8mg	0.37ml	6	7	9	11	8	6
4	280g	2.8mg	0.37ml	5	7	8	11	8	5
5	280g	2.8mg	0.37ml	5	6	9	12	8	5
6	290g	2.9mg	0.38ml	6	7	9	11	8	6

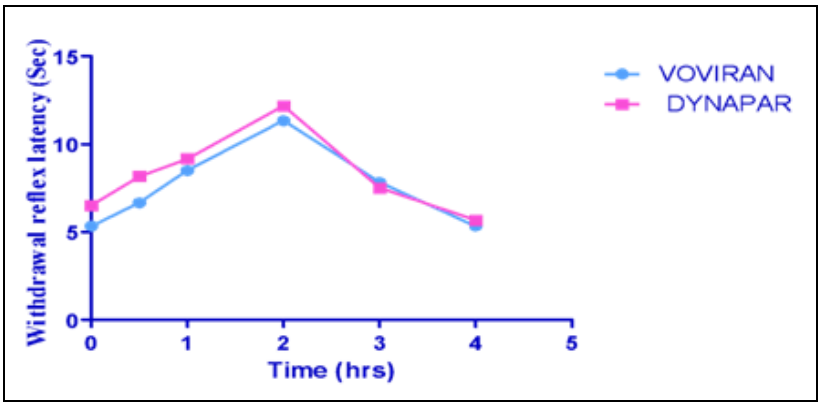

FIG. 2: COMPARISON OF VOVIRAN AND DYNAPAR DRUGS FOR ANALGESIC ACTIVITY BY INTRAPERITONEAL ROUTE OF ADMINISTRATION USING HOT PLATE METHOD IN RATS USING STUDENT T-TEST AT P<0.05.

An increase in reaction time is generally considered an important parameter of central and peripheral analgesic activity by non-selective COX inhibition and nociceptors. The hot-plate result showed a significant reduction of pain at 120 min following generic drug (VOVIRAN) compared to the branded drug (DYNAPAR) when given by the intraperitoneal route.

Evaluation of Anti- Inflammatory Activity by Intra Peritoneal Route of Administration:

TABLE 6: RANBAXY BRANDED DRUG, DOSE: 45mg TABLET BY INTRAPERITONEAL ROUTE USING DIGITAL PLETHYSMOMETER IN RATS

S. no	Body weight (gms)	Dose (mg)	Dose (ml)	Carrageenan induced paw volume (ml)	0 min (ml)	30 min (ml)	1 h (ml)	2 h (ml)	3 h (ml)	4 h (ml)
1	200	2	0.8	1.47	0.50	1.0	1.35	1.20	0.92	0.92
2	220	2.2	0.88	1.14	0.76	1.25	1.44	1.17	1.08	0.88
3	240	2.4	0.96	1.31	0.50	1.14	1.47	1.00	0.79	0.70
4	240	2.4	0.96	1.42	0.51	1.15	1.49	1.21	0.79	0.79
5	220	2.2	0.88	1.37	0.47	1.29	1.42	1.12	0.95	0.92
6	210	2.1	0.84	1.44	0.53	1.27	1.31	1.07	0.85	0.85

TABLE 7: INTAGESIC GENERIC DRUG, DOSE: 75mg AM PULE BY INTRAPERITONEAL ROUTE USING DIGITAL PLETHYSMOMETER METHOD IN RATS

S. no.	Body weight (gms)	Dose (mg)	Dose (ml)	Carrageenan induced paw volume (ml)	0 min (ml)	30 min (ml)	1 h (ml)	2 h (ml)	3 h (ml)	4 h (ml)
1	280	2.8	0.37	1.14	1.08	1.29	1.50	1.44	1.00	0.85
2	280	2.8	0.37	0.38	1.44	1.04	1.29	1.14	0.90	0.82
3	280	2.8	0.37	1.70	0.96	1.20	1.38	1.20	0.85	0.95
4	280	2.8	0.37	0.98	0.65	1.31	1.59	1.38	0.97	0.93
5	280	2.8	0.37	0.79	0.53	1.15	1.56	1.25	0.99	0.95
6	280	2.8	0.37	1.81	1.95	1.07	1.62	1.37	0.83	0.81

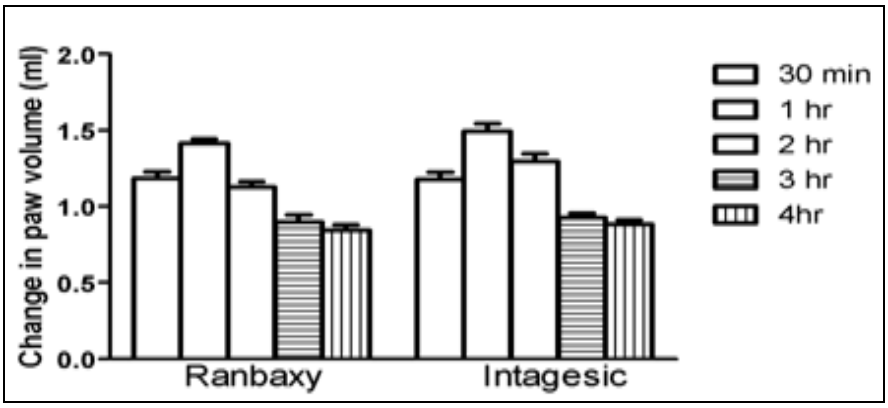

FIG. 3: COMPARISON OF RANBAXY AND INTAGESIC DRUGS FOR ANTI-INFLAMMATORY ACTIVITY BY INTRAPERITONEAL ROUTE OF ADMINISTRATION USING DIGITAL PLETHYSMOMETER IN RATS USING STUDENT T-TEST AT P<0.05

In the carrageenan-induced inflammation model, branded drug (RANBAXY) showed a significant decrease in paw volume when compared to carrageenan-induced rat paw volume. Generic drugs (INTAGESIC) were administered 30 min prior to carrageenan showed dose-dependent anti-inflammatory activity by reducing paw volume. Generic drug Intagesic showed a significant reduction of as paw volume when compared to branded drug Ranbaxy group when given by intraperitoneal route.

TABLE 8: DYNAPAR BRANDED DRUG, DOSE: 75mg AMPULE BY INTRAPERITONEAL ROUTE USING DIGITAL PLETHYSMOMETER METHOD IN RATS

S. no.	Body weight (gms)	Dose (mg)	Dose (ml)	Carrageenan induced paw volume (ml)	0 min (ml)	30 min (ml)	1 (ml)	2 h (ml)	3 h (ml)	4 h (ml)
1	300	3	0.4	1.41	0.91	1.47	1.44	1.32	1.12	0.92
2	300	3	0.4	0.92	0.75	0.98	1.55	1.26	1.08	0.88
3	320	3.2	0.42	1.08	0.96	1.08	1.61	1.35	0.96	0.78
4	290	2.9	0.38	1.02	0.72	1.47	1.65	1.21	1.02	0.98
5	300	3	0.4	1.05	0.65	0.92	1.75	1.37	1.11	0.91
6	310	3.1	0.41	1.08	0.93	1.08	1.39	1.12	0.95	0.81

TABLE 9: VOVERANGENERIC DRUG, DOSE: 75mg AM PULE BY INTRA PERITONEAL ROUTE USING DIGITAL PLETHYSMOMETER METHOD IN RATS

S. no.	Body weight (gms)	Dose (mg)	Dose (ml)	Carrageenan induced paw volume (ml)	0 min (ml)	30 min (ml)	1 h (ml)	2 h (ml)	3 h (ml)	4 h (ml)
1	280	2.8	0.37	1.08	0.85	1.38	1.41	1.20	0.85	0.85
2	290	2.9	0.38	1.67	0.89	1.70	1.52	1.10	1.08	0.88
3	280	2.8	0.37	1.70	0.65	1.00	1.20	1.03	0.67	0.67
4	280	2.8	0.37	1.52	0.78	1.51	1.59	1.08	0.89	0.85
5	280	2.8	0.37	1.67	0.96	1.14	1.20	1.05	0.97	0.97
6	290	2.9	0.38	1.21	0.82	1.21	1.81	1.00	0.85	0.85

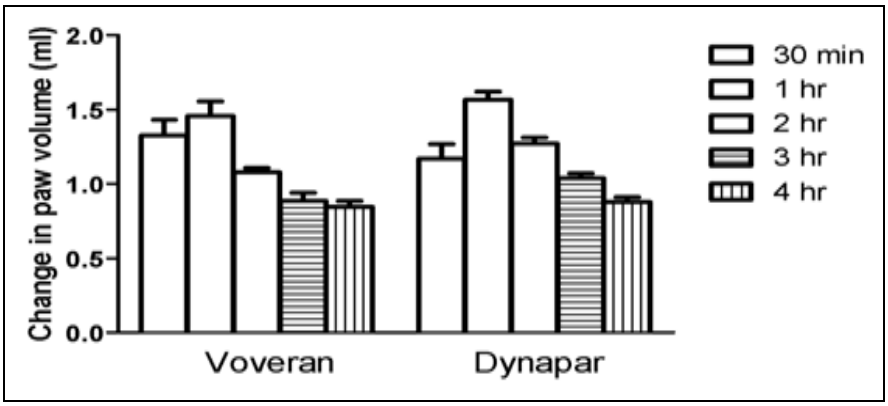

FIG. 4: COMPARISON OF VOVERAN AND DYNAPAR DRUGS FOR ANTI-INFLAMMATORY ACTIVITY BY INTRAPERITONEAL ROUTE OF ADMINISTRATION USING DIGITAL PLETHYSMOMETER IN RATS USING STUDENT T-TEST AT P<0.05

Both branded drugs (DYNAPAR) and generic drugs (VOVERAN) showed dose-dependent anti-inflammatory activity. Voveran showed significant anti-inflammatory activity by reducing carrageenan-induced paw volume compared with Dynapar when administered intraperitoneal route.

Evaluation of Analgesic Activity by Oral Route of Administration:

TABLE 10: CIPLA BRANDED DRUG, DOSE: 10mg TABLET BY ORAL ROUTE USING HOT PLATE METHOD IN RATS

S. no.	Body weight (gms)	Dose (mg)	Dose (ml)	0 min (sec)	30 min (sec)	1 h (sec)	2 h (sec)	3 h (sec)	4 h (sec)	5h (sec)
1	280	2.8	0.37	5	6	6	8	10	9	6
2	290	2.9	0.38	5	7	7	8	10	8	7
3	280	2.8	0.37	6	6	6	7	10	8	6
4	280	2.8	0.37	5	7	7	8	10	8	7
5	280	2.	0.37	5	7	7	9	11	9	7
6	290	2.9	0.38	6	6	6	8	11	9	6

TABLE 11: DICOLIV GENERIC DRUG, DOSE: 50mg TABLET BY ORAL ROUTE USING HOT PLATE METHOD IN RATS

S. no.	Body weight (gms)	Dose (mg)	Dose (ml)	0 min (sec)	30 min (sec)	1 h (sec)	2 h (sec)	3 h (sec)	4 h (sec)	5h (sec)
1	200	2	0.8	7	6	6	8	10	7	5
2	220	2.2	0.88	5	5	5	6	8	6	5
3	240	2.4	0.96	8	6	6	8	10	8	6
4	240	2.4	0.96	8	5	5	7	9	7	5
5	220	2.2	0.88	5	5	5	7	9	6	5
6	210	2.1	0.84	7	5	5	6	8	6	5

The Hot plate method is useful in elucidating centrally mediated antinociceptive responses, which focuses mainly on changes above the spinal cord level.

The generic drug (CIPLA) significantly ($p<0.05$) reduced the pain as compared to the branded drug (DICOLIV) when administered by oral route.

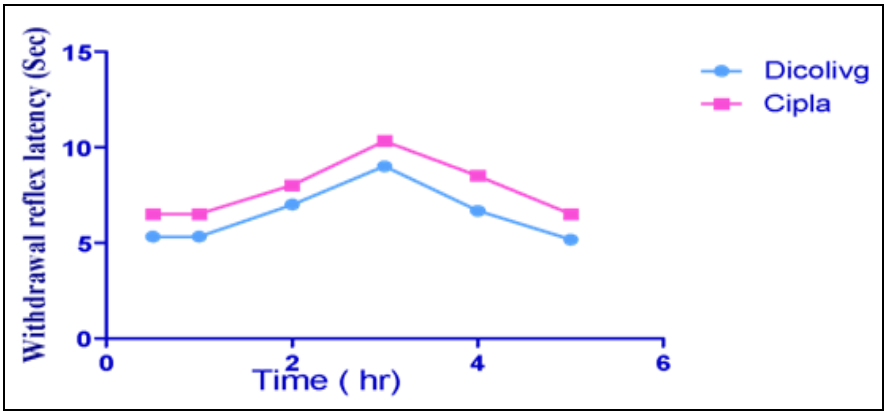

FIG. 5: COMPARISON OF CIPLA AND DICOLIV DRUGS FOR ANALGESIC ACTIVITY BY ORAL ROUTE OF ADMINISTRATION USING HOT PLATE METHOD IN RATS USING STUDENT T-TEST AT P<0.05.

TABLE 12: RANBAXY BRANDED DRUG, DOSE: 45mg TABLET BY ORAL ROUTE USING HOT PLATE METHOD IN RATS

S. no.	Body weight (gms)	Dose (mg)	Dose (ml)	0 min (sec)	30 min (sec)	1 h (sec)	2 h (sec)	3 h (sec)	4 h (sec)	5h (sec)
1	280	2.8	0.37	7	7	7	8	10	8	7
2	280	2.8	0.37	5	6	6	8	9	8	6
3	280	2.8	0.37	8	6	6	7	9	8	6
4	280	2.8	0.37	8	7	7	9	10	9	7
5	280	2.8	0.37	5	7	7	8	10	9	7
6	280	2.8	0.37	7	6	6	8	10	9	6

TABLE 13: VOVIRIN GENERIC DRUG, DOSE: 100mg TABLET BY ORAL ROUTE USING HOT PLATE METHOD IN RATS

S. no.	Body weight (gms)	Dose (mg)	Dose (ml)	0 min (sec)	30 min (sec)	1 h (sec)	2 h (sec)	3 h (sec)	4 h (sec)	5h (sec)
1	300	3	0.4	9	6	6	7	10	8	5
2	300	3	0.4	5	6	6	8	10	8	5
3	320	3.2	0.42	5	7	7	9	11	10	6
4	290	2.9	0.38	5	6	6	8	10	8	6
5	300	3	0.4	6	7	7	8	10	9	6
6	310	3.1	0.41	8	6	6	7	10	9	5

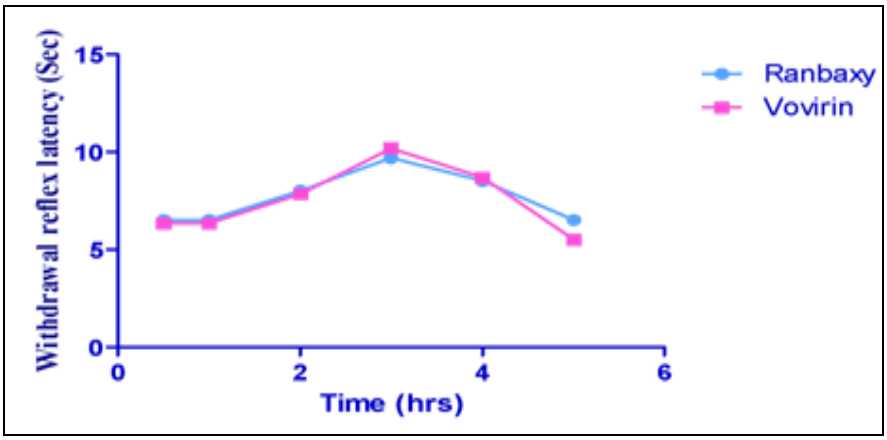

FIG. 6: COMPARISON OF RANBAXY AND VOVIRIN DRUGS FOR ANALGESIC ACTIVITY BY ORAL ROUTE OF ADMINISTRATION USING HOT PLATE METHOD IN RATS USING STUDENT T-TEST AT P<0.05

An increase in reaction time is generally considered an important parameter of central and peripheral analgesic activity by non-selective COX inhibition and nociceptors.

The hot-plate result showed a significant reduction of pain at 180 min following generic drug (VOVIRAN) compared to the branded drug (RANBAXY) when given by oral route.

Evaluation of Anti-Inflammatory Activity Oral Route of Administration:

TABLE 14: RANBAXY BRANDED DRUG, DOSE: 45mg TABLET BY ORAL ROUTE USING DIGITAL PLETHYSMOMETER IN RATS

S. no.	Body weight (gms)	Dose (mg)	Dose (ml)	Carrageenan induced paw volume (ml)	0 min (ml)	30 min (ml)	1 h (ml)	2 h (ml)	3h (ml)	4 h (ml)	5h (ml)
1	280	2.8	0.3	0.83	0.33	0.97	1.01	0.99	0.79	0.51	0.35
2	280	2.8	0.37	0.66	0.29	0.91	1.0	0.95	0.75	0.54	0.34
3	280	2.8	0.37	0.91	0.31	0.95	1.01	0.93	0.76	0.52	0.33
4	280	2.8	0.37	0.82	0.33	0.99	1.03	0.93	0.73	0.50	0.32
5	280	2.8	0.37	0.80	0.28	1.01	1.03	0.95	0.74	00.51	0.30
6	280	2.8	0.37	0.79	0.30	0.99	1.10	0.97	0.76	0.51	0.30

TABLE 15: DICLOV GENERIC DRUG, DOSE: 50mg TABLET BY ORAL ROUTE USING DIGITAL PLETHYSMOMETER METHOD IN RATS

S. no.	Body weight (gms)	Dose (mg)	Dose (ml)	Carrageenan induced paw volume (ml)	0 min (ml)	30 min (ml)	1 h (ml)	2 h (ml)	3 h (ml)	4 h (ml)	5 h (ml)
1	200	2	0.8	0.93	0.29	0.97	1.01	0.99	0.77	0.54	0.31
2	220	2.2	0.88	0.91	0.32	0.97	1.05	0.98	0.79	0.56	0.32
3	240	2.4	0.96	0.81	0.33	0.87	1.07	0.92	0.81	0.55	0.35
4	240	2.4	0.96	0.92	0.30	0.98	1.02	0.92	0.75	0.62	0.33
5	220	2.2	0.88	0.93	0.32	0.97	1.01	0.93	0.78	0.59	0.32
6	210	2.1	0.84	0.91	0.31	0.99	1.03	0.95	0.79	0.56	0.34

TABLE 16: CIPLA BRANDED DRUG, DOSE: 10mg TABLET BY ORAL ROUTE USING DIGITAL PLETHYSMOMETER IN RATS

S. no	Body weight (gms)	Dose (mg)	Dose (ml)	Carrageenan induced paw volume (ml)	0 min (ml)	30 min (ml)	1 h (ml)	2 h (ml)	3h (ml)	4 h (ml)	5 h (ml)
1	200	2	0.8	0.68	0.38	0.91	1.01	0.97	0.89	0.68	0.39
2	220	2.2	0.88	0.78	0.41	0.95	1.03	0.99	0.90	0.65	0.43
3	240	2.4	0.96	0.81	0.39	0.97	1.01	0.99	0.89	0.70	0.41
4	240	2.4	0.96	0.82	0.37	0.92	1.02	1.01	0.95	0.61	0.39
5	220	2.2	0.88	0.81	0.40	0.90	1.01	0.97	0.90	0.64	0.40
6	210	2.1	0.84	0.80	0.41	0.89	1.03	0.98	0.89	0.60	0.39

TABLE 17: VOVERAN GENERIC DRUG, DOSE: 100mg TABLET BY ORAL ROUTE USING DIGITAL PLETHYSMOMETER IN RATS

S. no.	Body weight (gms)	Dose (mg)	Dose (ml)	Carrageenan induced paw volume (ml)	0 min (ml)	30 min (ml)	1 h (ml)	2 h (ml)	3h (ml)	4 h (ml)	5h (ml)
1	300	3	0.4	0.77	0.29	0.97	1.0	0.99	0.82	057	0.30
2	300	3	0.4	0.77	0.32	0.97	1.02	0.95	0.80	0.60	0.31
3	320	3.2	0.42	0.87	0.30	1.07	1.07	0.99	0.83	0.55	0.32
4	290	2.9	0.38	0.82	0.33	1.08	1.08	1.0	0.86	0.60	0.34
5	300	3	0.4	0.97	0.34	1.10	1.10	1.0	0.80	0.60	0.32
6	310	3.1	0.41	0.97	0.32	1.12	1.12	1.01	0.82	0.59	0.35

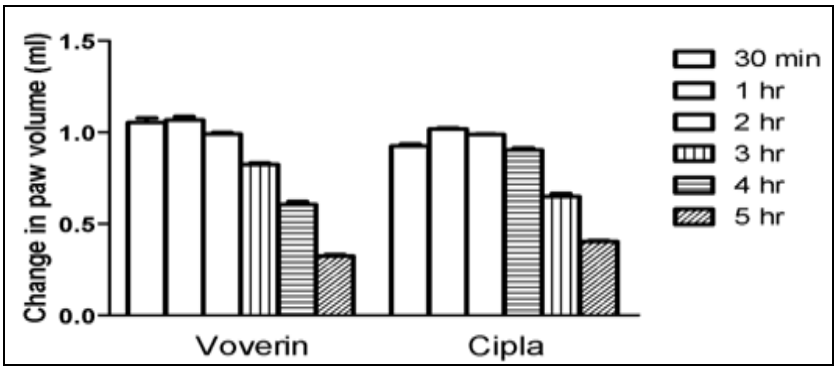

FIG. 8: COMPARISON OF CIPLA AND VOVERIN DRUGS FOR ANTI-INFLAMMATORY ACTIVITY BY ORAL ROUTE OF ADMINISTRATION USING DIGITAL PLETHYSMOMETER IN RATS USING STUDENT T-TEST AT P<0.05

Both branded drugs (CIPLA) and generic drugs (VOVERIN) showed dose-dependent anti-inflammatory activity. Voveran showed significant anti-inflammatory activity by reducing carrageenan-induced paw volume when compared with Cipla when given by oral route.

DISCUSSION: The difference between branded and generic drugs is considered as one of the major issues for governments, pharmacists, physicians, and patients. In addition to the difference in cost, there are varieties of opinions on the efficacy of generics versus brands. With this view, the present experiments have been undertaken to evaluate the efficacy of the brand (Voveran, Dynapar and Cipla) and genetics (Ranbaxy, Intagesic, and Diclovin) of diclofenac-sodium. Diclofenac is a potent non-steroidal anti-inflammatory drug (NSAID) effective in treating pain and inflammation in various acute and chronic conditions. Diclofenac is a sodium or potassium salt of phenylacetic acid derivative. The drug can target the deep inflamed tissues like joints preferentially and can accumulate 20 times more when compared to plasma. This is due to its weakly acidic nature, low volume of distribution and its high protein binding capacity.

AS with all NSAIDs, the mechanism of action of diclofenac is due to the suppression of prostaglandin (PG) synthesis through inhibition of cyclo-oxygenase (COX) enzyme that catalyzes the conversion of arachidonic acid into thromboxane and prostacyclin. Diclofenac oral formulations which have been demonstrated as effective are being used widely for over 30 years and are generally well tolerated. When used at high doses for prolonged periods, these may cause systemic side effects in some patients**.** This study evaluated the anti-inflammatory and analgesic effects of diclofenac sodium using Eddy's hot plate model and the Plethysmometer model. The effect of the diclofenac brand form was compared to the generic form by intraperitoneal and oral routes of administration. In this study, the anti-inflammatory and analgesic effects of diclofenac-sodium is used to evaluate the anti-inflammatory effects; carrageenan-induced acute rat paw edema was used a sensitive inflammatory model, which is commonly used. In parallel, to evaluate the analgesic effect, brewer's yeast-induced rat paw hyperalgesia was used as an inflammatory analgesia model. Our study demonstrated that Ranbaxy, Intagesic and Diclovin were comparable to the brand of diclofenac-sodium (Voveran, Dynapar and Cipla) in hot plate test and plethysmometer. However, the analgesic activity of Ranbaxy, Intagesic, and Voveran at Ind and 2th h was significantly ($p<0.05$) equal to Dynapar, Diclovin, and Cipla. Also, it was found that all the four generics suppressed nociceptive effects more potently ($p<0.05$) compared to Dynapar, Diclovin, and Cipla at 3th hour, but after 3 h, the analgesic activity of Dynapar increased and there is no significant ($p>0.05$) difference between Dynapar, Diclovin and Cipla and the other generics, also at 30 min and 1 h. The variation in the results between these products may be related to the difference in pharmaceutics parameters or bioavailability of the drugs.

There was no significant difference between Ranbaxy, Intagesic, Voveran, Dynapar, Diclovin, and Cipla in all phases of the formalin test. Thus, this study's result supports the theory reported in different studies, which is generic drugs did not differ from their brand in terms of efficacy. In the early phase of the formalin test, it was found that all study groups significantly reduced the number of flinching and jerking (Pd”0.05) compared to the control group, but the duration of licking was not significant in all groups of diclofenac-sodium. Rosland *et al.* reported that anti-inflammatory drugs didn't affect the initial phase of the formalin test even with a very low concentration of formalin. Our findings support these results as well.

Again, the results of licking duration were not significantly lower in treatment groups compared to the control group ($p>0.05$), but the difference between these groups in the frequency of jerking was statistically significant. Thus, this study states that both Generic and Branded drugs have the same effect. So, Generic drugs can be used instead of Branded drugs.

CONCLUSION: The generic and branded drugs studied in this research project met the pharmacopoeial requirements. The generic drugs Ranbaxy, Intagesic and Diclovin and the Branded drugs Voveran, Dynapar, and Cipla showed the same Analgesic activity and anti-inflammatory activity at the same time intervals.

This study concluded that both generic and branded drugs had shown the same efficacy, and there is no difference between the branded and generics.

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CONFLICTS OF INTEREST: Nil

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