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ANTI-NOCICEPTIVE EFFECT OF SELECTED BRANDS OF IBUPROFEN TABLETS OBTAINED FROM PHARMACEUTICAL STORES IN ADAMAWA STATE

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ABSTRACT

Ibuprofen is a widely used nonsteroidal anti-inflammatory drug (NSAID) for pain management. However, concerns exist regarding the quality and consistency of medications available in low- and middle-income countries (LMICs). This study investigated the anti-nociceptive effect of commercially available ibuprofen tablets obtained from pharmaceutical stores in Adamawa State, Nigeria. The samples were tested on laboratory animals (Rats) using the Hot plate method to determine their potency and therapeutic efficacy. The results showed that there was an increase in reaction time at all the treatment times for all the samples when compared to baseline values (0 min) within the same treatment groups. In comparison to the saline-treated animals, there was a significant increase in the reaction time to thermal pain detectable in sample brand E, except in sample brand A which has the lowest reaction time at 30min treatment time. However, the same trend was also observed using the percentage Maximum Possible analgesia (MPA%), the sample brand E also elicited significant analgesic activity within 30min following treatment as evidenced by the gradual increase throughout the observation period and at peak activity (30min), the sample showed MPA of 70.64%, while animals treated with sample brand A exhibited the lowest analgesic effect which gradually increases from 0min treatment time with MPA of 7.61%, and at 30min treatment time with MPA of 44.46%, therefore, the study concluded that the sample brands E could be classified as the most potent and effective amongst all the samples analyzed. This information can inform regulatory authorities, healthcare professionals, and consumers about the potential variations in pain management effectiveness.

Keywords: Ibuprofen, Anti-nociceptive effect, Dissolution profile, Sub-standard medications, Pain management.

1. INTRODUCTION

Pain is a complex physiological and psychological experience that significantly impacts human health and well-being (Basbaum et al., 2020). It is the leading symptom prompting individuals to seek medical attention, and its management is a critical aspect of healthcare delivery (Smith et al., 2021). Nociception, the neural processing of potentially damaging stimuli, underlies the subjective experience of pain (Julius & Basbaum, 2020). Therefore, therapeutic interventions targeting nociceptive pathways are essential for effective pain management. Ibuprofen, a nonsteroidal anti-inflammatory drug (NSAID), is one of the most

widely used medications globally for its analgesic and anti-inflammatory properties (McIvor et al., 2020). Its mechanism of action primarily involves the inhibition of cyclooxygenase (COX) enzymes, which are responsible for prostaglandin synthesis, key inflammatory mediators that sensitize nociceptors (Ferland, 2021). Prostaglandins also contribute to fever and inflammation, making ibuprofen a valuable therapeutic option for various pain conditions, including musculoskeletal pain, headache, and dysmenorrhea (Tatum *et al*., 2020).

The analgesic efficacy of ibuprofen is well-established, with numerous clinical trials and observational studies demonstrating its effectiveness in managing acute and chronic pain (Maruti et al., 2020; Moore et al., 2020). Ibuprofen is available over-the-counter (OTC) in various formulations, including tablets, capsules, liquids, and gels, making it accessible to a large population (Tatum et al., 2020). This widespread availability, coupled with its perceived safety profile compared to other NSAIDs, has contributed to ibuprofen's immense popularity as a self-medication choice for pain management (McIvor *et al*., 2020).

However, concerns regarding the quality and consistency of medications available in low- and middle-income countries (LMICs) have emerged (World Health Organization, 2020). Factors such as weak regulatory frameworks, inadequate quality control measures, and the prevalence of counterfeit drugs can significantly impact the efficacy and safety of medications like ibuprofen (World Health Organization, 2019). This is particularly concerning for medications like ibuprofen, where even minor variations in formulation or active ingredient content can affect its therapeutic effectiveness (Kareem *et al*., 2021).

Nigeria, a populous nation in West Africa, is classified as a lower-middle-income country (World Bank, 2023). Despite significant economic growth in recent decades, access to quality healthcare remains a challenge for many Nigerians (Afolabi *et al*., 2020). The pharmaceutical sector in Nigeria is vast and complex, with a mix of registered and unregistered outlets dispensing medications (Afolabi *et al*., 2021). While regulations exist to govern the sale and distribution of medications, enforcement remains a challenge, potentially allowing for the +0020 healthcare and the potential presence of substandard medications (Federal Ministry of Health Nigeria, 2021). Ibuprofen is a commonly used medication in Adamawa for pain management, and its availability across various pharmaceutical outlets raises concerns about the drug's quality and consistency.

This research study investigated the potency and therapeutic efficacy (in laboratory animals) of the Ibuprofen 400mg tablets in some selected brands of Ibuprofen 400mg tablet formulations commercially available in the Nigerian market obtained in some pharmaceutical stores in Adamawa state, by using Hot plate test method. This study's findings will contribute valuable insights into the quality and efficacy of commercially available ibuprofen tablets in Adamawa State. By evaluating the in vitro dissolution profiles and anti-nociceptive activity of different brands, this research can provide information on the consistency and effectiveness of these medications in managing pain.

2.0 MATERIALS AND METHOD

2.1 Equipment and Reagents

The apparatus and equipment used are analytical balance, 250-g capacity (Resolution 0.0001g) glass wares, pestle and mortar, water bath, thermometer, surface probe thermometer, temperature recorder, stopwatch/ Time recorder, Hot plate apparatus,

disposable 0.45 µm filters, Hypodermic syringe, cotton wool, transparent plastic cage and measuring cylinder, as well as Samples brands and pure laboratory standard Ibuprofen and Normal saline which was used as blank.

The equipment and apparatus used in this study were calibrated to check their status before and in the middle of the experiments. Apparatus such as volumetric flasks, measuring cylinders, and other glass/plastic ware were thoroughly washed with detergents and tap water and then rinsed with deionized water. All glassware was cleaned with 10% concentrated Nitric acid (HNO3) to clear out any heavy metal on their surfaces and then rinsed with distilled-deionized water, the reagents used are methanol, and HNO_3.

2.2 Samples and Sampling Method

The standard Ibuprofen crystals were obtained from Pharmaceutical Vendors, all other chemicals were of analytical grade, and deionized water was used in all experiments.

Ten commercially available sample brands of Ibuprofen tablets each with a label claim of 400mg were randomly selected and purchased from the selected retail pharmaceutical stores, in Adamawa state, the samples were blindly labeled as Sample A (A), Sample B (B), Sample C (C), Sample D (D) and Sample E (E), Sample F (F), Sample G (G), Sample H (H), Sample I (I), Sample J (J) and used as samples.

Table 1: Label Information of Sample Brands of Ibuprofen Tablets

S/N	Sample Code	Label Claim (mg)	Expiry Date
1	A	400mg	October 2026
2	B	400mg	August 2024
3	C	400mg	August 2024
4	D	400mg	March 2025
5	E	400mg	June 2026
6	F	400mg	January 2026
7	G	400mg	January 2025
8	H	400mg	March 2026
9	I	400mg	June 2026
10	J	400mg	April 2026

2.3 Selection of Laboratory Animals for determination of Antinociceptive effect

48 rats of either sex were obtained from the Biochemistry Department, MAU, Yola, the rats were 6 weeks old and weighed between 90gm and 120gm at the onset of the experiment. They were handled and kept under typical laboratory conditions (temperature 22°C±2°C;) for

two days to acclimatize and to ensure normal behavior. The rats were held in plastic cages and fed on a balanced diet (soybeans and maize meal).

2.4 Preparation of standard and Sample Solutions for Anti-nociceptive effects

A standard working solution was prepared by dissolving 20 mg of the pure laboratory standard Ibuprofen Crystals in 100 ml of deionized water, from which a 200 standard working solution was prepared. 10 tablets of each brand of Ibuprofen were accurately weighed and crushed uniformly with the help of a mortar and pestle, weighed sample powder equivalent to 20 mg of each brand of Ibuprofen was transferred into a volumetric flask and made-up volume to 100 ml with deionized water, from which a working solution of 200ppm each was prepared.

2.5 Hot Plate Test

Evaluation of the Anti-Nociceptive (analgesic) activity of the extract was carried out using the hot plate method, (Sook-Ha *et al*., 2014), the rats were randomly arranged into twelve groups, four rats per group, the dose of both the standard and sample per rats was calculated based on the body weight of each rat used, the solutions were injected intraperitoneally using a disposable syringe and needle at a calculated dose of 60mg/kg, the control group was administered with normal saline (10ml/kg).

The rats were placed on a hot plate maintained at 55±l°C within the restrainer. The reaction time (in seconds) or latency period was determined as the time taken for the rats to react to the thermal pain by licking their paws or jumping. The reaction time was recorded before (0 min) and at 15, 30, 45, and 60min after the administration of the samples. The maximum reaction time was fixed at 45sec to prevent any injury to the tissues of the paws, readings exceeding 45sec were considered as maximum analgesia. (Sook-Ha *et al*., 2014).

A stopwatch was used to record the reaction time (i.e., the time interval between dropping the rat on the hot plate and jumping off the hot plate).

The effects of Ibuprofen, on the pain response time were recorded, the experiment showed that rats exhibit different levels of pain responses at a set temperature at different doses of Ibuprofen by behavioral changes such as paw padding(shaking), paw licking and jumping (Giglio *et al*., 2006). The reaction time in all the groups was recorded and comparisons were made on the time response between those rats in the control group, the rats that received the pure standard Ibuprofen, and those that received the sample brands of Ibuprofen.

2.6 Statistical Data Analysis

The data was generated and the results were evaluated by charts and tables and expressed as a mean standard deviation ± SD and standard error mean (SEM), which was used to make comparisons for the quantitative and qualitative assay as well as the anti-nociceptive activities of the sample brands of the Ibuprofen tablets, a probability of $P < 0.05$ was considered as significant. Thus, the Maximum Possible Analgesia (MPA):

$$MPA = \frac{\text{Reaction time for treatment - Reaction time for Normal saline}}{\text{45 Seconds - Reaction time for normal saline}} \times 100$$

3.0 RESULTS AND DISCUSSION

Table 1: Anti-nociceptive effect (Analgesic) of sample brands of Ibuprofen extract using Hot plate method on Rats

	Reaction time in seconds (Mean ± SEM)				
Samples/Treatment	**0mins**	**15mins**	**30mins**	**45mins**	**60mins**
Normal saline	07.66 ± 0.39	10.08 ± 0.25	13.49 ±0.52	14.99 ± 0.23	13.58 ± 0.46
Pure Sample	14.55 ± 0.38	23.02 ± 0.32	37.01 ± 0.22	34.08 ± 0.15	30.13 ± 0.51
Sample A	10.50 ± 0.65	19.25 ± 0.48	27.50 ±0.96	30.00 ± 0.71	25.50 ± 0.50
Sample B	11.00 ± 0.41	20.00 ± 0.41	30.00 ± 0.41	31.00 ± 1.47	25.25 ± 0.95
Sample C	11.75 ± 0.48	20.00 ± 0.41	31.00 ±0.71	29.25 ± 0.48	25.75 ± 0.63
Sample D	12.25 ± 0.75	19.00 ± 0.41	28.75 ± 0.75	31.25 ± 0.48	27.50 ± 0.50
Sample E	13.50 ± 0.96	21.50 ± 0.50	35.75 ± 1.54	28.00 ± 1.22	24.50 ± 0.87
Sample F	10.75 ± 0.25	20.00 ± 0.71	30.00 ± 0.41	32.25 ± 1.11	27.00 ± 0.82
Sample G	10.25 ± 0.48	20.00 ± 0.41	29.25 ± 0.48	31.00 ± 0.71	27.00 ± 0.71
Sample H	12.00 ± 0.58	19.00 ± 0.71	28.50 ± 0.65	27.00 ± 1.22	21.50 ± 1.32
Sample I	10.75 ± 0.25	20.00 ± 0.41	31.00 ± 0.71	28.50 ± 0.65	25.75 ± 0.48
Sample J	10.75 ± 0.48	20.00 ± 0.41	29.25 ± 0.25	31.25 ± 0.25	27.00 ± 0.41

Table 2: Maximum Possible Analgesia of sample brands of Ibuprofen extract using Hot plate method on Rats

	Maximum Possible Analgesia (MPA%)				
Samples/Treatment	**0mins**	**15mins**	**30mins**	**45mins**	**60mins**
Pure Sample	18.62	35.94	75.87	63.02	52.67
Sample A	7.61	26.26	44.46	50.01	37.93
Sample B	8.94	28.41	52.39	53.34	37.14
Sample C	10.95	28.41	55.56	47.51	38.73
Sample D	12.29	25.54	48.42	54.18	44.33
Sample E	15.64	32.71	70.64	43.35	34.75
Sample F	8.27	28.41	52.39	57.51	42.71
Sample G	6.94	28.41	50.01	53.34	42.71
Sample H	11.62	25.54	47.64	40.01	25.21
Sample I	8.27	28.41	55.56	45.01	38.73
Sample J	8.27	28.41	50.01	54.18	42.71

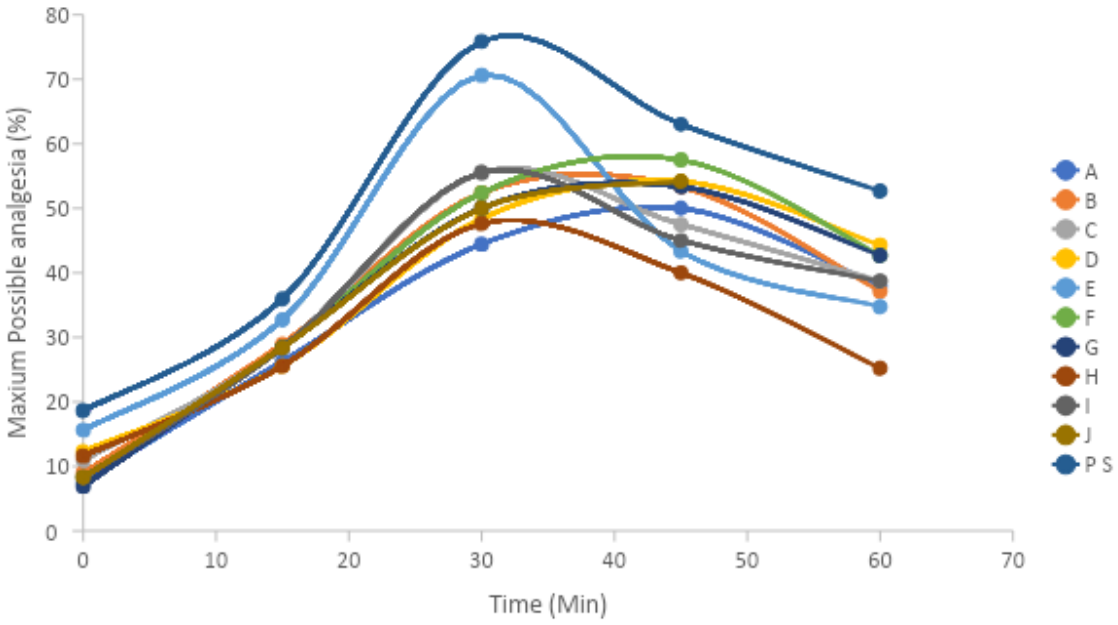

Figure 1: Anti-nociceptive effect (Analgesic) (MPA%) of Sample brands of Ibuprofen tablets by Hot plate method on Rats.

DISCUSSION

Anti-nociceptive effect (Analgesic effect) of Sample Brands of Ibuprofen Tablets using Hot plate test on Rats.

The results of the Analgesic effect of the sample brands of Ibuprofen tablets (Samples A-J) using the hot plate method are presented in Table 1, Table 2, and Figure 1, The results showed that there was an increase in reaction time at all times points compared to baseline values (0 min) within the same treatment groups. In comparison to the saline-treated animals, the significant increase in the reaction time to thermal pain was detectable in sample brand E, except in sample brand A which has the lowest reaction time at 30min treatment time. However, the same trend was also observed using the Maximum Possible analgesia (MPA%), sample brand E also elicited significant analgesic activity within 30min following treatment as evidenced by the gradual increase throughout the observation period, at peak activity (30min), the sample showed MPA of 70.64%, while animals treated with sample brand A exhibited the lowest analgesic effect which gradually increases from 0min treatment time with MPA of 7.61% and peak activity at 30min with MPA of 44.46%.

The results also showed that the analgesic effect (%MPA) of the sample brands of Ibuprofen at 30min treatment time decreases in the order as follows: Sample brand E > sample brand C&I > sample brand B&F > sample brand G&J > sample brand D > sample brand H > sample brand A.

In all sample brands, their analgesic effect gradually declined after 30min treatment time, and at 45min, which was considered to be the maximum reaction time to avoid injury to the tissues of the paws, the lowest MPA (40.1%) was recorded in the sample H.
The reaction times were significantly different between all samples at 30, 45, and 60 min after treatment.

CONCLUSION

The anti-nociceptive study showed an analgesic effect where the reaction time increases at different treatment times by all the samples, the study revealed that sample brand E showed the highest percentage maximum possible analgesia (70.64%), while sample brand A showed the lowest percentage maximum possible analgesia (44.46%).

It is expected that samples with the highest drug concentration should elicit the maximum analgesic effect as shown by the (MPA%) of the pure standard sample (75.87%), therefore, this suggests that there is a direct correlation between the concentration of the drug with its activity or effectiveness. Based on this, the study will go further to conclude that sample brand E has the highest potency and effectiveness as compared to other sample brands analyzed.

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