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RESEARCH ARTICLE

FOOD AND DRUG INTERACTION WITH IBUPROFEN TABLET

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ABSTRACT

The aim of this work was to study all possible food-drug interactions and weather the drug should take before or after the breakfast. This study was carried out by using Ibuprofen tablet (500mg) and different Indian breakfasts of different regions like Idali sambhar, Pohe, Paratha, Misal Pav, Wadapav and Egg Omelette. Three healthy Volunteers were selected for this study and they were allowed to take Ibuprofen tablet before breakfast and after breakfast in consecutive two days. The urine samples were collected at regular intervals from volunteers and further elimination rate constant (KE) was calculated from urinary excretion data. Excretion of Ibuprofen was affected by composition of breakfast, timing of tablet administration. It also shows inter-subject variation. The rate of excretion was observed higher for breakfast egg omelette containing lower Carbohydrate, lower fat and higher protein. The rate of excretion was observed higher when tablet has taken after breakfast.

Key words: Ibuprofen, Analgesic,Food drug interaction, Cumulative amount excreated, Sigma minus method.

INTRODUCTION

Non-Steroids anti-inflammatory drugs, usually abbreviated to NSAIDs or NAID, are drug with analgesic, antipyretic and, in higher doses,anti-inflammatory effects-they reduce pain, fever& inflammation. The term “non-steroidal” is used to distinguish these drugs from steroids, which (among a broad range of other effects) have a similar eicosanoid-depressing ,anti-inflammatory action. As analgesic, NSAIDs are unusual in that they are non-narcotic. NSAIDS are sometimes also referred to as non-steroidal anti-inflammatory agent/analgesic (NSAIAs) or non-steroidal anti-inflammatory medicines (NSAIMs).The most prominent members of this group of drugs are aspirin, ibuprofen, and naproxen partly because they are available over the counter in many areas.

Most NSAIDs are weak acids, with a pKa of3-5. They are absorbed well from the stomach and intestinal mucosa. Most NSAIDs are metabolized in the liver by oxidation and conjugation to inactive metabolites which are typically excreted in urine.

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Drug Food Interaction:-

The effect produced when some drugs and certain foods or beverages are taken at the same time. For example, grapefruit juice blocks the metabolism of some drugs in the GI tract, an action that can cause normal dosages of a drug to reach toxic levels in the plasma.

OR

The pharmacological result, either desirable or undesirable, of drugs interacting with components of the diet.

Need of Work:-

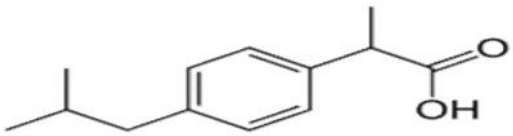
- To avoid the interaction
- To give better relief effect
- It Show high GI tolerability like Selectively Cox-2 inhibiter
- No Adverse effect cardio vascular system
- Ibuprofen is NSAID drug which acts on inflammation side

It is highly effective and decreases the inflammation

DRUG PROFILE

Ibuprofen[1,2,3,]

- **Chemical structure**

Molecular formula  **Ibuprofen $C_{13}H_{18}O_2$ [2]**

Ibuprofen (iso-butyl-propanoic-phenolicacid) is a non-steroidalanti-inflammatory drug (NSAID) originally marketed as Brufen, and under various other trademarks Nurofen, Advil and Motrin. It is used for relief of symptoms of arthritis, primary dysmenorrhea, fever, and as an analgesic, especially where there is an inflammatory component.

Ibuprofen is known to have an antiplatelet effect, though it is relatively mild and short-lived when compared with that of aspirin or other better-known antiplatelet drugs. Ibuprofen is a core medicine in the World Health Organization's "Essential Drugs List", which is a list of minimum medical needs for a basic health care system.

Description: White crystalline powder or colorless crystals, odorless

- **Solubility:** Freely soluble in acetone, in chloroform, in Ethanol (95%) & in ether, practically insoluble in water. It dissolves in dilute solution of alkali hydroxides & carbonate
- **Mol. Mass:** 206.3 gm/mole
- **Melting Point**: 76^0c
- **Dose:** 600 mg to 149-73% Hepatic 1.8-2hrs
- **Routes:** Renal Oral, Rectal and topical

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- **Bioavailability**: 49-73%
- **Half-Iife**: 2-4 hrs
- **Excretion:** Renal
- **Standard**: S*C* Ibuprofen contains not less than 98.5% & not more 101.0% of calculated with reference to thedried substance.
- **Storage:** Store in well-closed container

History of Ibuprofen [4,5]

Ibuprofen was developed by the research arm of Boots Group during1960s20. It was discovered by Stewart Adams, with colleagues Clive McMahon, Jeff Bruce Wilson, Andrew RM Dunlop and Colin Burrowpatented in 1961. The drug was launched as a treatment for rheumatoid arthritis in United Kingdom in 1969, and in the United States in 1974. Famously, it is recorded that Dr. Adams initially tested his drug on a hangover. He was subsequently awarded in 1987.

Off-label and investigational use:

- Ibuprofen is sometimes used for the treatment of acneinflammatory properties, and has been sold in Japan in topical term for adult acne
- As with other NSAIDs. Ibuprofen may be useful in the treatment of severe orthostatic hypotension (low blood pressure when standing up).
- In some studies, ibuprofen showed superior results compared to placebo In the prophylaxis of Alzheimer's disease, when given in low doses over a long time"". Ibuprofen has been associated with a lower risk of ParVdnaon'sdiacise, and may delay or prevent Parkinson's disease. Aspirin, other NSAlOa, and paracetamol had no effect on the risk for Parkinson's** .Further research is warranted before recommending ibuprofen for this use.

Mechanism of action [6,7]

Ibuprofen is an NSAID which is believed to work through inhibition of cyclooxygenase (COX), thus inhibiting prostaglandin synthesis. There are at least 2 variants of cyclooxygenase (COX-1 and COX-2). Ibuprofen inhibits both COX-1 and COX-2. It appears that its analgesic, antipyretic, and anti-inflammatory activity are achieved principally through COX-2 inhibition; whereas COX-1 inhibition is responsible for its unwanted effects on platelet aggregation and the GI mucosa. The role of the individual COX iso forms in the analgesic, anti-inflammatory, and gastric damage effects of NSAIDs is uncertain and different compounds cause different degrees of analgesia and gastric damage26.

Adverse effects [8,9]

Ibuprofen appears to have the lowest incidence of gastrointestinal adverse drug reactions (ADRs) of all the non-selective NSAIDs. However, this only holds true at lower doses of ibuprofen, so over-the-counter preparations of ibuprofen are generally labeled to advise a maximum daily dose of 1,200 mg. Common adverse effects include; nausea, dyspepsia,

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gastrointestinal ulceration/bleeding, raised liver enzymes, diarrhea, epistaxis, headache, dizziness, unexplained rash, salt and fluid retention, and hypertension. Infrequent adverse effects include esophageal ulceration, heart failure, hyperkalaeinia, renal impairment, confusion, bronchospasm, and rash.

- Risks in pregnancy
- Risks in Inflammatory Bowel Disease (IBD)
- Cardiovascular risk:

MATERIALS USED

Ibuprofen tablet

Tablet	: Ibuprofen 400 mg
Brand Name	: Brufen
Manufacturer By	: Abbott
Batch No	: 21804D7
Manufacturer Date	: 09/2012
Expiry Date	: 08/2015
No. Of Tablet	: 60

Buffer solution [2]

- Phosphate Buffer Solution PH 7.2
- 0.2M Potasiumdihydrogen phosphate:
- 0.2M NaOH Solution**:**

Indian Breakfast

1. Poha
2. Idli Sambar
3. Aaloo Paratha
4. Vada Pav
5. Misal
6. Egg Ommlette

EQUIPMENTS AND INSTRUMENTS USED:[10,11]

- **Dissolution test apparatus:** Made by- Electrolab 8 Station
  Model no. TDL- 08L
- **Disintegration Test:**
- **UV Visible spectrophotometer:** Model no. Shimadzu- 1800
- **Ultrasonicator:** Ultrasonic frequencies (> 20 kHZ) are used.

EXPERIMENTAL THEORY:

In-vitro study[2]

- **Dissolution test:**
- **Disintegration Test:**

In-vivo study [12]

- **Urinary Excretion Method**

Volunteers urine samples were collected at specific time intervals like 2,4,6,8…up to 24 hrs. The collected samples were diluted properly with distilled water and their absorbance was

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calculated. From the absorbance values further their drug concentrations were calculated. Further their Elimination rate constant (K_E) values were calculated by using two methods-They are as below

1. Cumulative amount Method[1]
2. Sigma minus method[1]

Volunteer's Selection:

Chosen Volunteers were examined by Dr. Beri and after obtaining certificate to their fitness for this study, following pattern was adapted-

Breakfasts	**Days**	**Events**
Pohe	1st Day	Pohe + Ibuprofen Tablet
	2nd Day	Ibuprofen Tablet +Pohe
Idalisambar	1st Day	Idalisambar + Ibuprofen Tablet
	2nd Day	Ibuprofen Tablet +Idalisambar
Alooparatha	1st Day	Alooparatha + Ibuprofen Tablet
	2nd Day	Ibuprofen Tablet + Alooparatha
Wadapav	1st Day	Wadapav + Ibuprofen Tablet
	2nd Day	Ibuprofen Tablet + Wadapav
Misal	1st Day	Misal + Ibuprofen Tablet
	2nd Day	Ibuprofen Tablet +Misal
Egg Ommlette	1st Day	Egg Ommlette + Ibuprofen Tablet
	2nd Day	Ibuprofen Tablet + Egg Ommlette

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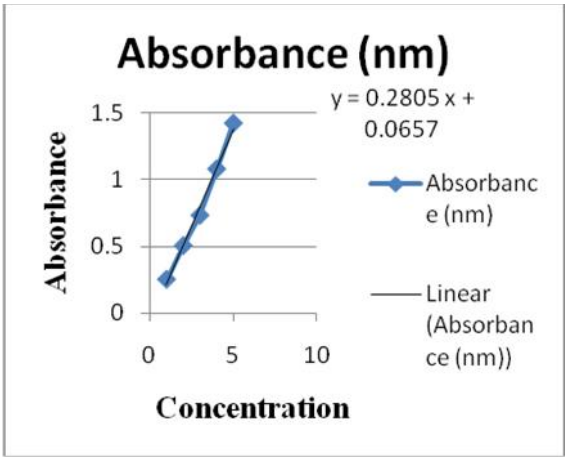
RESULT AND DISCUSSION

Calibration pure Ibuprofen drug in urine

Concentration	Absorbance (nm)
1	0.252
2	0.504
3	0.731
4	1.079
5	1.421



Dissolution test

Table 1 Calibration of pure Ibuprofen drug in phosphate buffer pH 7.2

Conc Mcg	Absorbance
1	0.048
2	0.069
3	0.088
4	0.115
5	0.132

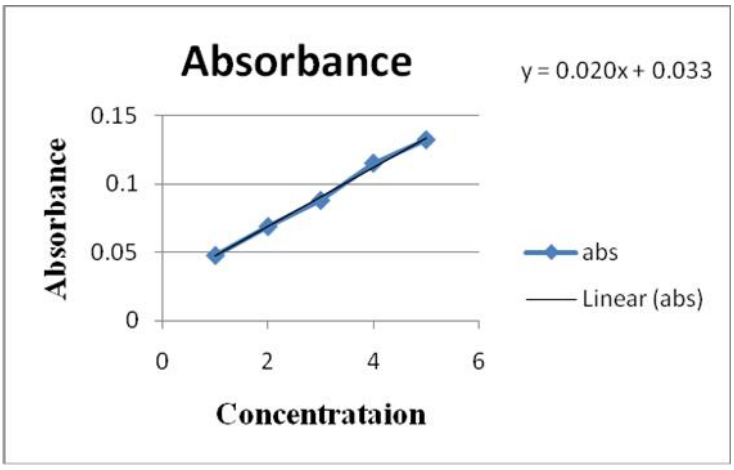


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Table 2 Dissolution of Ibuprofen 500 mg tablet in phosphate buffer pH 7.2

Tablet	Absorbance	Concentration	dilution	Volume (ml)	Concentration mcg	Concentration mg	% Release
1	0.262	11.45	458	900	412200	412.2	82.44
2	0.269	11.80	472	900	424800	424.8	84.96
3	0.278	12.25	490	900	441000	441.0	88.20
4	0.276	12.15	486	900	437400	437.4	87.48
5	0.280	12.35	494	900	444600	444.6	88.92
6	0.283	12.50	500	900	450000	450.0	90.00

Table 3 Percentage Dissolution of Ibuprofen Tablet:

Tablet	**% release**
1	82.44
2	84.96
3	88.20
4	87.48
5	88.92
6	90.00

Disintegration test

Disintegration time of Ibuprofen tablet (500 mg) was found to be15 second.

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Table 4: Values of K_E(Elimination rate constant) by cumulative amount excreted: (volunteers wise)

Volunteers Name	Poha		Idalisambar		Alooparatha		Vadapav		Misal		Egg Ommlette	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
Volunteer1	0.5020	0.1594	0.2304	0.1618	0.2465	0.9416	0.1033	0.5104	0.0558	0.1548	0.0993	0.4251
Volunteer2	0.0849	0.3343	0.5382	0.2570	0.2978	0.2978	0.1033	0.5104	0.0889	0.4545	0.1299	1.5455
Volunteer3	0.0849	0.3343	0.1244	1.5408	0.2890	0.0453	0.3773	0.0454	0.3646	0.5070	0.1708	0.3180

Table 5: Values of K_E(Elimination rate constant) by cumulative amount excreted: (Breakfast wise)

Volunteers Name	Volunteer1		Volunteer2		Volunteer3	
	Before Breakfast	After Breakfast	Before Breakfast	After Breakfast	Before Breakfast	After Breakfast
Poha	0.5020	0.1594	0.0849	0.3343	0.0849	0.3343
Idalisambar	0.2304	0.1618	0.5382	0.2570	0.1244	1.5408
Alooparatha	0.2465	0.9416	0.2978	0.2978	0.2890	0.0453
Vadapav	0.1033	0.5104	0.1033	0.5104	0.3773	0.0454
Misal	0.0558	0.1548	0.0889	0.4545	0.3646	0.5070
Egg Ommlette	0.0993	0.4251	0.1299	1.5455	0.1708	0.3180

Table 6 Cumulative amount of unchanged drug(Volunteers wise)

Volunteers Name	Poha		Idalisambar		Alooparatha		Vadapav		Misal		Egg Ommlette	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
Volunteer1	68	22.57	123.40	79.28	108	108	100.86	45.76	72.19	45.76	86.39	46.29
Volunteer2	11.87	100.24	90.72	133.34	71.13	71.13	61.1	56.95	64.35	102.28	64.72	39.96
Volunteer3	122.01	24.23	108.92	136.30	139.96	139.96	152.29	86.95	65.48	78.29	64.58	46.01

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Table 7 Cumulative amount of unchanged drug (breakfast wise)

Volunteers Name	Volunteer1		Volunteer2		Volunteer3	
	Before Breakfast	After Breakfast	Before Breakfast	After Breakfast	Before Breakfast	After Breakfast
Poha	68	22.57	11.87	100.24	122.01	24.23
Idalisambar	123.40	79.28	90.72	133.34	108.92	136.30
Alooparatha	108	108	71.13	71.13	139.96	139.96
Vadapav	86.39	45.76	61.1	56.95	152.29	86.95
Misal	72.19	45.76	64.35	102.28	65.48	78.29
Egg Ommlette	86.39	46.29	64.72	39.96	64.58	46.01

Table 8 Values of K_E by (Sigma-minus Method) (Volunteers wise)

Volunteers Name	Poha		Idalisambar		Alooparatha		Vadapav		Misal		Egg Ommlette	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
Volunteer1	0.1658	0.2233	0.2072	0.2256	0.2210	0.1980	0.1566	0.1911	0.2095	0.1842	0.1566	0.2026
Volunteer2	0.2049	0.1151	0.2326	0.1934	0.2003	0.2004	0.1681	0.2006	0.2118	0.1888	0.1519	0.1980
Volunteer3	0.1427	0.1865	0.2210	0.1980	0.2026	0.2326	0.1865	0.2187	0.1934	0.1889	0.1681	0.1842

Table 9 Values of $K_E$by sigma minus method (breakfast wise)

Volunteers Name	Volunteer1		Volunteer2		Volunteer3	
	Before Breakfast	After Breakfast	Before Breakfast	After Breakfast	Before Breakfast	After Breakfast
Poha	0.1658	0.2233	0.2049	0.1151	0.1427	0.1865
Idalisambar	0.2072	0.2256	0.2326	0.1934	0.2210	0.1980
Alooparatha	0.2210	0.1980	0.2003	0.2004	0.2026	0.2326
Vadapav	0.1566	0.1911	0.1681	0.2006	0.1865	0.2187
Misal	0.2095	0.1842	0.2118	0.1888	0.1934	0.1889
Egg Ommlette	0.1566	0.2026	0.1519	0.198	0.1681	0.1842

CONCLUSION

Excretion of Ibuprofen is affected by composition of breakfast, timing of tablet administration. It also shows inter-subject variation.

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The rate of excretion is higher for breakfasts as omelette containing lower carbohydrate, lower fat and higher proteins.
Also rate of excretion is higher when tablet is taken after breakfast.

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