In Vitro Comparative Quality Assessment of Different Brands of Ibuprofen Tablet Available in Bangladesh

A Project Report Submitted to the Department of Pharmacy, Jahangirnagar University in Partial Fulfillment of the Requirements for the Degree of Bachelor Pharmacy

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JAHANGIRNAGAR UNIVERSITY

SAVAR, DHAKA-1342, BANGLADESH

DEDICATED TO

My Beloved Parents!

CERTIFICATE:

This is to certify that the work entitled '*In Vitro* Comparative Quality Assessment of Different Brands of Ibuprofen Tablet Available in Bangladesh', a comprehensive laboratory based research, submitted to the Department of Pharmacy, Jahangirnagar University in partial fulfillment of the requirements for the degree of B. Pharm. (Professional) was carried out by Md. Mamunur Roshed (Exam. Roll No.:171795, Reg. No: 45219) in the Department of Pharmacy, Jahangirnagar University under my direct guidance and supervision.

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DECLARATION

I hereby declare that this work entitled '*In Vitro* Comparative Quality Assessment of Different Brands of Ibuprofen Tablet Available in Bangladesh' submitted to the Department of Pharmacy, Jahangirnagar University in partial fulfillment of the requirements for the degree of B. Pharm. (Professional) was carried out by me under the guidance of Dr. Mohammad Didare Alam Muhsin, Professor, Department of Pharmacy, Jahangirnagar University, Savar, Dhaka. I also declare that this work has not been submitted for any other degree.

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I give thanks to the Almighty, who has enabled everything in my life. It is He who has kept me going while I have been studying.

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ABSTRACT

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID) that possesses anti-inflammatory, analgesic, and antipyretic effects and it is widely manufactured and marketed in the Republic of Bangladesh. This study focused on *in vitro* evaluation of two brands of conventional ibuprofen tablet dosage forms of 400 mg strength available in the local market of Bangladesh. As per various public and private publications and records, there are more licensed brands of the drug, but currently only these two brands are in active supply in the local market. Although the product is also available in 200 mg strength, the 400 mg strength was chosen for this work because according to market sources this is the most prescribed strength of the drug. The quality control parameters, commonly used for the evaluation of tablet products, *viz.*, organoleptic properties, thickness and diameter, hardness, friability, weight & weight variation, disintegration time, assay and dissolution profile, were studied. For the most purpose, The United States Pharmacopeia (USP) methods and specifications were followed for conducting the tests and drawing inferences. The tablets studied here were white in color and oblong in shape. None of them, however, had any odor. The diameter and thickness of the products studied did not meet the criterion for all the units being within ±5% of average. The only exception was the product, F-400's diameter, which was within the acceptable range. The average hardness of F-400 was 9.8±0.234kg/cm^2, which meets the requirement of being above 4 kg/ cm^2. However, the other product, A-400 failed to meet this requirement for hardness (3.28±0.074 kg/cm^2). The friability of the products was 0.215% (A-400) and 0.146% (F-400), both of which were within the acceptable limit of not more than 1%. For A-400, the maximum upper and lower weight variations were 2.573% and 3.185%, respectively, while for F-400, the corresponding figures were 1.728% and 1.532%, respectively. Thus, in terms of the weight variation, both the products met the USP requirement of being within ± 5% for tablets weighing >324 mg. The disintegration times for the products, both in water and acid (0.1N HCl), was well below the acceptable limit of 30 minutes for film coated tablets. The brand A-400 showed a potency of 98.450% and F-400 a potency of 94.637% when assayed in 0.1N NaOH. Both the products met the USP allowance of not exceeding 110% and not being less than 90%. On the other hand, however, the *in vitro* drug release from both the brands in phosphate buffer (pH 7.2) was around 60% only, which was below the USP requirement of not less than 80% in 60 min for

Ibuprofen Tablets. To conclude, both the products studied in this work consistently performed well in *in vitro* evaluation in terms of almost all the parameters tested. The only major concern observed was the dissolution rate which needs to be addressed. There are some concerns with the uniformity of diameter and thickness of the products and with the hardness of one product as well. The results of this work can provide useful guidance to health professionals as well as consumers. In addition, the manufacturers and the regulatory authorities can also use this data for their purposes. Further studies with more samples from different batches are warranted to draw a more conclusive inference.

Keywords: Ibuprofen, Tablet, Quality, *In Vitro*, Comparative, Hardness, Assay, Disintegration, Dissolution.

Aims & Objectives of the Work

Aims of the work:

This work was set out with the following aims:

- To assess *in vitro* the quality of the Ibuprofen tablet products available in the local market.
- To compare the quality of different brands of the product available.
- To provide the manufacturers an overview of the quality of the products marketed by them and help them to pinpoint the issues need to be addressed for further upgrading the quality.
- To assure health care providers and consumers of the quality of the products and their interchangeability.

Objectives of the Work:

To achieve above aims, following objectives were set for the work:

- To assess *in vitro* various physical parameters used in the evaluation of the quality of tablet products including organoleptic properties, thickness, diameter, hardness and friability.
- To assess the average weight and weight variation as a primary step towards ensuring the unit-to-unit and batch-to-batch uniformity.
- To perform the assay of the products for ensuring the presence of adequate amount of the drug in the dosage form.
- To perform disintegration and dissolution tests to ensure adequate release of drug at an appropriate rate when the tablets are administered and come in contact with the GI fluid.
- To compare different brands in terms of above quality parameters to ensure their comparability and interchangeabilit

Chapter 1: Introduction

Product quality in the pharmaceutical sector is critical to its long-term viability. A great degree of managerial, scientific, and technological skill is evident in it. Not only is quality required by government and regulatory agencies, but it is also essential for customer trust, especially when it comes to life-saving medications. To ensure quality, strict adherence to international safety, environmental, and regulatory requirements must be followed from the very beginning of the product manufacturing process. Additionally, pharmaceutical quality management requires validation.

Every pharmaceutical product must satisfy quality parameters since, in the absence of quality, there might be problems such as subtherapeutic or overdose effects that may prevent pharmaceuticals from being marketed or sold. A medicine with inadequate quality control may also cause patients to have dangerous side effects, some of which may be deadly. Ibuprofen is a commonly used NSAID that has to be carefully monitored for quality. Ibuprofen's formulation and bioavailability have a major role in how well it works as an active medication to treat pain and inflammation. Changes in the drug release patterns caused by substandard ibuprofen tablets might affect not only the duration and overall effectiveness of the treatment but also its onset and duration of effects.

Bangladesh may have limited access to healthcare services, thus it is essential to ensure the quality of pharmaceutical items, such as ibuprofen tablets. The quality of the various brands of ibuprofen tablets that are sold in Bangladesh has to be evaluated for a number of reasons. Preserving patients' health and treatment results is the first benefit; it ensures that pharmaceuticals are administered in accordance with performance and quality requirements. Furthermore, it fosters responsible drug use and the best possible patient care by supporting medical practitioners in making decisions about prescription and therapy management. Third, it enhances public health and trust in the healthcare system by supporting regulatory authorities in monitoring and enforcing adherence to pharmaceutical standards and regulations.

Comparing the in vitro quality attributes of many brands of ibuprofen tablets available in Bangladesh is the aim of this study. By examining important factors such dissolving profiles, disintegration durations, and medication content homogeneity, this study seeks to identify any discrepancies in product quality and usability. The findings will contribute to efforts to guarantee that everyone has access to high-quality, safe, and effective medications as well as deepen our understanding of Bangladesh's pharmaceutical industry.

1.1 Quality:

Any firm that wants to succeed and grow must prioritize quality. It is an indicator of a product or service's excellence that is assessed according to how satisfied customers are with it in relation to their needs. The ability of a product to satisfy the requirements and expectations of the consumer is referred to as its quality. To begin with, quality needs to be defined in terms of particular characteristics or criteria that change based on the kind of product. For example, medications are evaluated according to physical and chemical properties, efficacy, safety, taste, and shelf life, whereas mechanical or electronic devices are evaluated according to performance, dependability, safety, and attractiveness. Similar to this, food items are assessed based on a variety of criteria, including flavor, shelf life, nutritional content, and texture.

1.1.1 Components of the quality of a drug/ drug product

Important components of high-quality drugs/ drug products include:

- **Identity:** To avoid confusion or mistakes with other prescriptions, the drug's genuine identity and form must be made evident on the label.
- **Purity:** The drug must not include any ingredients that could jeopardize its efficacy or safety.

- **Safety:** There should be little chance of toxicity or unfavorable consequences, a balanced risk-benefit ratio, and the drug being safe to use.
- **Potency:** The active pharmaceutical ingredient (API) must be present in the amount indicated on the label in order for the drug to be effective.
- **Efficacy:** When administered in accordance with the recommended dose and indications, the medicine should exhibit the expected therapeutic effect.
- **Consistency:** It is imperative for pharmaceutical products to maintain consistent and uniform quality features throughout production facilities, formulations, and batches.

Guidelines and standards are established by regulatory bodies like the Food and Drug Administration (FDA) in USA, the European Medicines Agency (EMA) in Europe, and Directorate General of Drug Administration (DGDA) in Bangladesh to guide quality assurance and control procedures during the phases of drug development, manufacturing, and distribution. This helps to maintain public health, build confidence in the healthcare system, and make it easier for patients to obtain safe and effective medications.

1.1.2 *In Vitro* Quality Assessment of Tablets

Following is a brief outline of various aspects and parameters considered in the *in vitro* quality assessment of tablet products:

- **Appearance:** It is important to ascertain that the tablet is consistent in size, shape, and color and is free of chips, cracks, and discoloration.
- **Packaging Integrity:** It is essential to assure that the package is undamaged and that the batch number, expiration date, and manufacturer's information are properly labeled.
- **Physical Characteristics:** To make sure that the tablet can survive stresses of handling and shipping without shattering or would not disintegrate to fast or too slow, its thickness, hardness, and friability should be checked.
- **Chemical Composition:** To verify that active pharmaceutical ingredients (APIs) are present and there are no contaminants, analytical methods like spectroscopy or chromatography may be used.

- **Disintegration Time (DT):** The DT should be checked to make sure that the tablet will break down into smaller particles within the expected time-frame when it is exposed to the GI fluid after administration.
- **Potency Determination (Assay):** It is important to make sure that the tablet contains adequate amount of the active ingredients compared to the label claim.
- **Uniformity of Dosage:** To make sure that the dose is the same across the batch, weight variation and content uniformity checks need to be performed.
- **Dissolution Study:** The tablet should be subjected to an appropriated dissolution study to ascertain that it dissolves at an appropriate rate and to the desired extent that will ensure adequate bioavailability.
- **Microbiological Purity:** To make sure the tablet satisfies the requirements for microbial contamination, microbiological limit testing should be performed.
- **Stability Testing:** The tablet's shelf life should be assessed under different environmental conditions by conducting rapid and real-time stability testing.
- **Compliance with Regulatory Standards:** It should be ensured that the tablet meets the standards set by regulatory authorities such as the FDA or EMA regarding safety, efficacy, and quality.
- **Documentation and Record Keeping:** To ensure regulatory compliance and traceability, detailed records of all quality assessment procedures and outcomes should be preserved.
- **Adherence to Good Manufacturing Practices (GMP):** To ensure consistent tablet quality and safety, it is imperative to make sure that manufacturing procedures follow GMP criteria.

1.2 Non-steroidal Anti-inflammatory Drugs (NSAIDs)

1.2.1 History of NSAIDs

NSAIDs have a long history. In old days, willow bark was used to treat fever and pain since it contained salicin. Chemists extracted salicylic acid from willow bark in the 19th century, which paved the way for Charles Frederic Gerhardt to synthesize acetylsalicylic acid, or aspirin, in 1853. The contemporary NSAID era began in 1899 when Bayer registered aspirin as a trademark. As a

consequence of its ability to reduce pain and inflammation, NSAIDs such as ibuprofen (1961), indomethacin (1963), naproxen (1967) and diclofenac (1973) came in succession and became popular during the 20th century. NSAIDs continue to be crucial for treating pain, inflammation, and fever despite their side effect concerns. The term 'non-steroidal', which became popular about 1960, sets these medications, Nonsteroidal anti-inflammatory medicines, or NSAIDs, as a class of pharmaceuticals that are often used to treat fever, decrease inflammation, and relieve pain. The way they work is by preventing the body from producing prostaglandins, which are molecules that cause fever, discomfort, and inflammation. Aspirin, naproxen, celecoxib and ibuprofen are typical examples of NSAIDs. Depending on their strength and composition, these medications may be obtained over-the-counter or with a prescription.

NSAIDs have possible hazards even if they are useful in treating ailments including arthritis, headaches, menstrual cramps, and mild injuries. Extended or high-dose NSAID use may have adverse effects, including bleeding, ulcers in the gastrointestinal tract, damage of the kidneys, and an increased risk of cardiovascular problems. Because of this, it is essential to use NSAIDs carefully and under medical supervision, especially for those who already have health issues or are on other drugs.

1.2.2 General Structure and Properties of NSAIDs

In general, NSAIDs structurally consist of an acidic moiety (carboxylic acid, enols) attached to a planar, aromatic functionality. Some analgesics also contain a polar linking group, which attaches the planar moiety to an additional lipophilic group. The structure can be represented as follows:

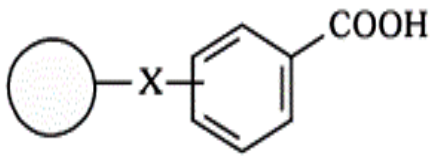


Figure 1.1: General Structure of NSAIDs

The NSAIDs can be sub-classified on the basis of chemical structure as Salicylates, Propionic Acids (Profens), Aryl and Heteroarylacetic Acids, Anthranilates (Fenamates), Oxicams (Enol Acids), Phenylpyrazolones, and Anilides.

Most of these compounds are carboxylic acids, which show significant ionization at physiological pH and may form salt when exposed to a base. Their ability to inhibit COX is dependent on the presence of the acidic group. Based on the lipophilic nature of their aryl groups as well as other lipophilic moieties and substituents, the NSAIDs have different lipophilicities.

The acidic group of these substances binds to plasma proteins primarily (ionic binding). By conjugation, the acidic group also functions as a key site of metabolism. As a result, glucuronidation (and inactivation) is a key mechanism of clearance for several NSAIDs, and therefore renal excretion.

1.2.3 Classification of NSAIDs

Based on the selectivity to the three isoforms of cyclooxygenase (COX) enzyme found in the body, *viz*. COX-1, COX-2 and COX-3, pharmacologically NSAIDs can be classified as follows:

Weak COX inhibitors: Choline Magnesium Trisalicylate, Sodium Salicylate, Olsalazine, Salsalate, Sulfasalazine.
COX-1/COX-2 inhibitors: Piroxicam, Sulindac, Indomethacin, Tolmetin, Ketorolac, Ibuprofen, Dexibuprofen, Fenoprofen, Carprofen, Flurbiprofen, Ketoprofen, Dexketoprofen, Naproxen, Loxoprofen, Oxaprozin, Diclofenac.
COX-2 preferential inhibitors: Nimesolid, Meloxicam.
COX-2 selective inhibitors: Celecoxib, Rofecoxib, Valdecoxib, Etorixocib, Lumiracoxib Firocoxib, Parecoxib.
COX-3 inhibitors: Acetaminophen.

1.2.4 Mechanism action of NSAIDs

The primary mechanism of action of Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) is the suppression of the cyclooxygenase (COX) enzymes, especially COX-1 and COX-2. By blocking COX enzymes NSAIDs prevent the synthesis of prostaglandins and thromboxanes from arachidonic acid. Prostaglandins and thromboxanes are implicated in pain, fever, inflammation, and platelet aggregation.

COX-1 is constitutively expressed in several tissues. It is engaged in preserving regular physiological processes including renal blood flow control, platelet aggregation, and gastrointestinal mucosal protection. COX-2 is primarily triggered during inflammation and promotes prostaglandin production, which is implicated in inflammation and discomfort.

Following is a brief account of how inhibition of COX enzymes and, in turn synthesis of prostaglandins and thromboxanes, leads to different NSAID effects:

- **Anti-inflammatory Effects:** NSAIDs decrease inflammation by reducing prostaglandin levels, which in turn reduces vasodilation, vascular permeability, and the recruitment of inflammatory cells to the site of injury or infection. Reduced heat, swelling, and redness are the outcomes of this reduction in inflammation.
- **Analgesic Effects:** NSAIDs reduce the sensitivity of peripheral pain receptors (nociceptors) to prostaglandins and other inflammatory mediators. They also prevent pain signals from reaching the central nervous system.
- **Antipyretic Effects:** By preventing prostaglandin production in the hypothalamus, the body's thermoregulatory center, NSAIDs have antipyretic (fever-reducing) effects. This area's prostaglandins raise the temperature of the hypothalamus, which causes fever.

It's important to understand that while NSAIDs may successfully reduce fever, inflammation, and pain, there may be dangers to the kidneys and gastrointestinal tract. Long-term NSAID usage increases the risk of bleeding, ulcers in the stomach, and problems with kidney function. Therefore,

it is recommended that people taking these drugs be cautious and seek medical advice, especially if they already have gastrointestinal or renal issues.

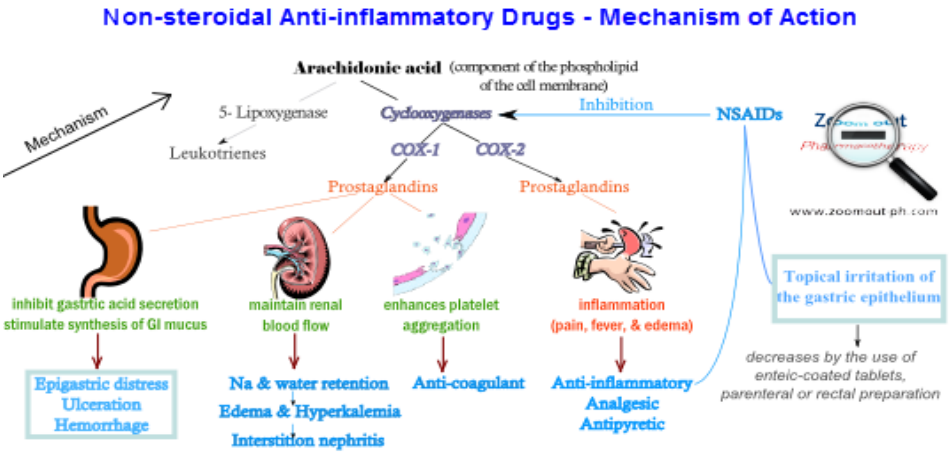


Figure 1.2: Mechanism action of NSAIDs

1.2.5 Indications of NSAIDs

- **Pain Relief:** Neural spasms, migraines, toothaches, cramps during menstruation, pains in the muscles, and pain from arthritis are all often treated with NSAIDs.
- **Anti-inflammatory:** They are used to lessen inflammation brought on by tendinitis, bursitis, arthritis, and other inflammatory diseases.
- **Fever Reduction:** NSAIDs work by affecting the hypothalamus, which is the part of the body that controls fever.
- **Dysmenorrhea:** NSAIDs are often used to treat menstrual cramps and discomfort.
- **Osteoarthritis and Rheumatoid Arthritis:** NSAIDs may help control the pain and inflammation brought on by both long-term joint disorders.
- **Gout:** To reduce pain and inflammation during gout episodes, NSAIDs could be useful.
- **Migraine:** When used alone or in conjunction with other drugs, NSAIDs may be helpful in treating migraine headaches.
- **Postoperative Pain:** NSAIDs are sometimes used in conjunction with other pain management techniques to treat postoperative pain.
- NSAIDs are often used to treat the pain and stiffness brought on by ankylosing spondylitis, an inflammatory disease that affects the spine.

To reduce the danger of side effects, it's important to take NSAIDs in accordance with suggested dosage and durations, under a doctor's supervision.

1.2.6 Contraindications of NSAIDs

NSAIDs should be used with caution by people with the following conditions:

- People over an age of 50 and who have a family history of gastrointestinal (GI) problems
- People with previous gastrointestinal problems from NSAID use.

NSAIDs should usually be avoided by people with the following conditions:

- Peptic Ulcer or stomach bleeding
- People with inflammatory bowel disease
- Uncontrolled hypertension
- Kidney disease
- Past transient ischemic attack
- Past stroke
- Past myocardial infraction
- Coronary artery disease
- Undergoing coronary bypass surgery
- Congestive heart failure
- In third trimester of pregnancy
- Persons who have undergone gastric bypass surgery
- Persons with a history of allergic or allergy like NSAID hypersensitivity reactions

1.2.7 Adverse reactions of NSAIDs

- **GI Side Effects:** By preventing prostaglandin production, which is essential for gastrointestinal protection, NSAIDs may irritate and inflame the stomach, intestines, and cause ulcers and bleeding.
- **Renal Effects:** Extended use of NSAIDs, particularly in those with pre-existing kidney problems, may cause damage to the kidneys, decreasing blood flow and compromising renal function.

- **Cardiovascular Risks:** NSAIDs may increase the risk of heart attack, stroke, and hypertension, especially in those who already have cardiovascular vulnerabilities. This risk is notably higher when the NSAIDs are used often or at high doses.
- **Hepatic Effects:** Although less frequent than other adverse responses, NSAIDs may cause liver damage, including hepatitis and liver failure. NSAIDs may cause allergic reactions in some people, which may range from minor skin rashes to life-threatening anaphylaxis.
- **GI Perforation:** If NSAID usage is severe, there is a risk of gastrointestinal perforation, which calls for emergency care.
- **Fluid Retention and Edema:** NSAIDs have the potential of causing edema and fluid retention, especially in those who have heart failure, are hypertensive, or have impaired kidney function.
- **CNS Effects:** Headaches, lightheadedness, and disorientation are uncommon side effects of NSAIDs, particularly in high dosages or in vulnerable people.
- **GI Strictures:** Long-term NSAID usage may cause gastrointestinal strictures, which may restrict the digestive track and possibly lead to blockage.
- **GI Bleeding:** The risk of gastrointestinal bleeding is increased by NSAIDs, particularly in older persons and those with a history of bleeding disorders or ulcers.

In order to reduce risks, it is important for NSAID users to be aware of these possible side effects and to take these drugs carefully and under medical supervision.

1.3 Profile of Ibuprofen --- the Drug under Study

1.3.1 History of ibuprofen

In the 1960s, Stewart Adams and John Nicholson of Boots UK made the discovery of ibuprofen. It was developed as a less harmful substitute for aspirin that has less adverse effects on the digestive system. In 1969, ibuprofen was approved by the FDA and made available on a prescription basis. It was made over-the-counter in the United States in 1983. Ibuprofen reduces inflammation, discomfort, and fever by blocking the actions of cyclooxygenase enzymes. It is one of the most popular nonsteroidal anti-inflammatory medications (NSAIDs) on the market today.

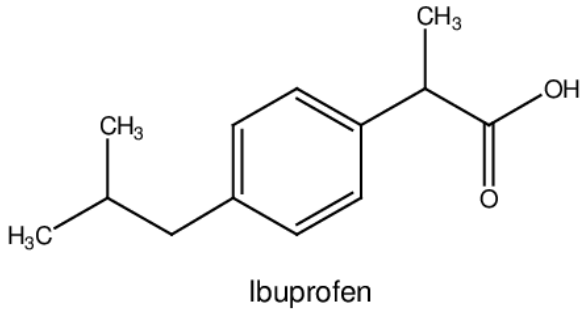


Figure 1.3: Structure of ibuprofen

1.3.2 Physicochemical Properties

Ibuprofen is a propanoic acid derivative having anti-inflammatory, analgesic, and antipyretic properties. Its chemical name is (2-[4-(2-methylpropyl) phenyl] propanoic acid). It has a benzene ring as a phenyl group attached to the second carbon of its three-carbon carboxylic acid functional group. The isobutyl group is para-positioned next to the propanoic group. S (+) ibuprofen has COX inhibitory action, and it is a racemic combination of R (-) and S (+) isomers. The key physicochemical properties of the drug are summarized below:

Molecular formula: $C_{13}H_{18}O_2$
Molecular weight: 206.285 g/mol
Melting point: 75-77° C
Solubility: 21 mg/L (at 25° C) in water, very soluble in alcohol and readily soluble in most organic solvents; low aqueous solubility at pH 1.2 and 4.5, high aqueous solubility at pH 6.8.
Partition coefficient (Log P): 3.97

Dissociation constant (pKa): 4.91
Biopharmaceutics Classification System (BCS): Class IIa (low aqueous solubility and high intestinal membrane permeability)
Appearnce: White crystalline powder.

These values can vary slightly depending on the source and conditions of measurement. So, good thing is to consult reliable sources or reference materials for specific information.

1.3.3 Pharmacology

1.3.3.1 Pharmacokinetics

Ibuprofen's pharmacokinetics may be summed up as follows:

Absorption: When taken orally, ibuprofen is quickly and effectively absorbed, reaching peak plasma concentrations in one to two hours. Food doesn't substantially change the rate of absorption; it can though delay it.

Distribution: Ibuprofen has a restricted extravascular distribution, as shown by its very modest volume of distribution. It is 99% or more protein bound to serum albumin. Ibuprofen enters the synovial fluid after passing through the blood-brain barrier.

Metabolism: Ibuprofen is extensively metabolized in the liver, mostly by cytochrome P450 enzymes such as CYP2C9 and CYP2C8 and to a lesser degree by CYP3A4. The two main metabolites, hydroxyibuprofen and carboxyibuprofen, are pharmacologically inert.

Elimination: In adults, ibuprofen has a half-life of two to four hours. Both renal and non-renal clearance processes are followed. About half of the overall clearance is removed via metabolism, with the other half coming from renal clearance.

Excretion: The majority of ibuprofen's and its metabolites' excretion occurs in the urine, whereby 50% to 60% of the dosage is within a day.

Special Populations: Older adults, those with renal impairment, and patients in pediatric settings may have different ibuprofen pharmacokinetics. Dosage modifications may be necessary due to longer elimination half-lives in the elderly and those with renal impairment. The pharmacokinetics in pediatric patients might change based on various factors including weight and age.

All things considered, ibuprofen is highly absorbed, heavily processed in the liver, and mostly eliminated in the urine. Comprehending its pharmacokinetic characteristics is crucial for maximizing treatment results and dosage considerations.

Here is a simplified account outlining some pharmacokinetic parameters of the drug:

Bioavailability: ~80-100%

Peak Plasma Time (T_{max}): 1-2 hours

Peak Plasma Concentration (C_{max}): 20-30 μg/mL

Plasma Half-life ($t_{½}$): ~2 hours

Volume of Distribution (V_d): 0.1-0.2 L/kg

Protein Binding: ~99%

Metabolism: Hepatic

Elimination: Renal (mainly as metabolites)

It may be worth noting here that these values can vary depending on factors such as dosage, formulation, and individual patient characteristics. So, it is always a good idea to consult a healthcare professional for accurate information regarding the use of the medication.

1.3.3.2 Pharmacodynamics

As an NSAID and propionic acid derivative, Ibuprofen works in a similar fashion as other classic NSAIDs in terms of its analgesic, antipyretic, and anti-inflammatory properties. Prostaglandin and thromboxane production is decreased as a result of its inhibition of cyclooxygenase I and II activity. Furthermore, by reducing the formation of thromboxane A2, ibuprofen prevents platelet aggregation.

1.3.3.3 Mechanism action of ibuprofen

Arachidonic acid is converted in the body to prostaglandin H2 by cyclooxygenase (COX), which is necessary for the production of prostaglandins via the arachidonic acid pathway. The inhibition of COX, which changes arachidonic acid into thromboxane A2, an essential element in platelet aggregation, is another way by which these effects are mediated. Because the maintenance of the gastric mucosa is disrupted, an excess of NSAID may result in the long-term inhibition of COX-1 and in turn may induce gastric toxicity.

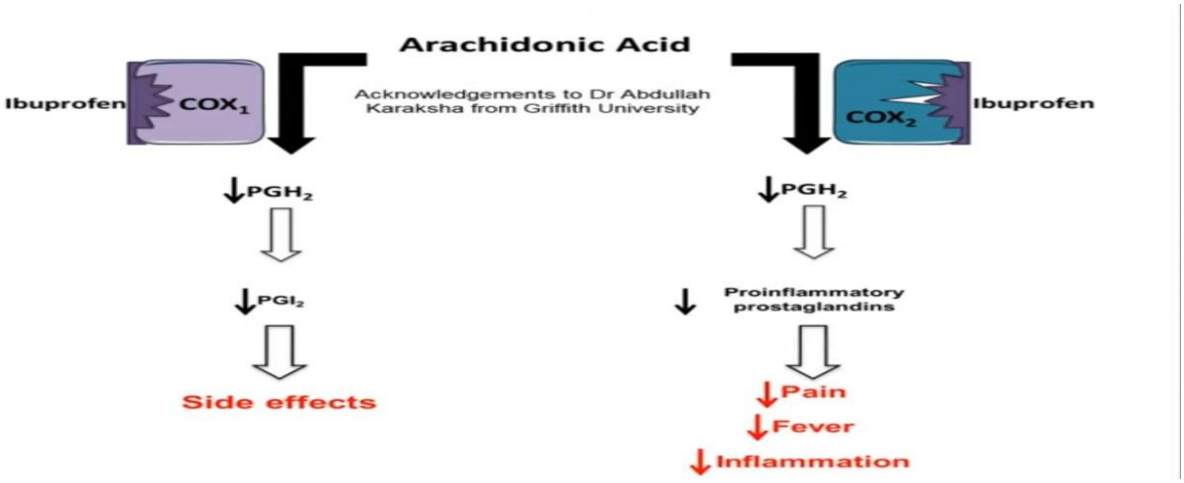


Figure1.4: Mechanism action of ibuprofen

1.3.4 Indications

Orthostatic hypotension: Ibuprofen, like other NSAIDs, may be helpful in treating severe orthostatic hypotension. Less than 100 mg/kg is unlikely to have toxic effects, but beyond that amount, it may have serious or perhaps fatal consequences.

Rheumatoid arthritis: Ibuprofen's potent anti-inflammatory and analgesic properties make it a popular choice for treating rheumatoid arthritis. It improves overall quality of life by reducing joint swelling, stiffness, and pain by blocking prostaglandin synthesis. But it is important to understand that ibuprofen just treats symptoms; it does not change how the illness progresses. For a full course of therapy, ibuprofen must be used in addition to other drugs like DMARDs.

Osteoarthritis: Ibuprofen's clinical effectiveness for osteoarthritis is similar to that of rheumatoid arthritis, although it has a somewhat superior therapeutic ratio of toxicity to effectiveness. Concerns over misuse for joints have been highlighted, even if an analgesic effect could appear more advantageous for osteoarthritis. At dosages above 1000 mg per day, ibuprofen is as effective as other NSAIDs at standard dosages, but it has less side effects, which is a distinct benefit.

Gout: Ibuprofen at a dosage of 2400 mg per day for three days effectively cured gout episodes in a recent trial including ten patients. It was believed that lower dosages were less beneficial.

Parkinsion's Disease: Two pathogenic pathways linked to Parkinson's disease (PD) include inflammation and oxidative stress. Regular use of NSAIDs, especially non-aspirin COX-2 inhibitors, was shown by epidemiologic research. PD risk is decreased by inhibitors like ibuprofen. Early and late phases showed a considerable induction of apoptosis, indicating that these anti-inflammatory drugs may prevent the growth of microorganisms.

Breast Cancer: The use of NSAIDs in breast cancer was studied by Harris *et al.* in 1999. Regular use of aspirin and ibuprofen reduced the incidence of breast cancer by around 40% and 50%, respectively.

Dental pain: As a popular nonsteroidal anti-inflammatory drug (NSAID) in dentistry, ibuprofen is used widely to treat orofacial discomfort that is either acute or chronic. The postoperative pain after third molar surgery may be effectively relieved with an ibuprofen dosage of 400 mg. When it comes to treating post-surgical dental pain, liquid gel formulations of ibuprofen at this dose show higher effectiveness and faster relief.

Cystic fibrosis (CF): It has also been shown that high-dose ibuprofen treatment reduces inflammation, most likely via reducing the infiltration of polymorphonuclear cells into the lungs. Patients with CF have a minimal risk of experiencing GI adverse effects from high dosage ibuprofen medication.

Prophylaxis of Alzheimer's Disease: The use of NSAIDs, especially ibuprofen, significantly lowered the rate of neurodegeneration. In some research, ibuprofen showed better outcomes than a placebo in the long-term, low-dosage prevention of Alzheimer's disease.

Other Uses of Ibuprofen:

- Ibuprofen, by inhibiting prostaglandin synthesis, effectively treats Bartter's syndrome, patent ductus arteriosus, and some recurrent abortion syndromes by reducing prostaglandin levels. Unlike other NSAIDs, ibuprofen is particularly effective for Bartter's syndrome.
- It is paradoxical that a research has recommended the use of ibuprofen for nephrosis, given the medication's documented effects on water and salt retention.
- According to a research, it is safe and effective for treating Still's illness.

1.3.5 Contraindications

Hypersensitivity to ibuprofen is a contraindication. In addition, ibuprofen should not be used in the following conditions:

- Gastrointestinal bleeding
- Active peptic ulcer
- Aspirin treatment
- Breastfeeding
- Neonates with congenital heart disease

According to a research on expectant mothers, consuming NSAIDs of any kind or dosage—including ibuprofen, diclofenac, and naproxen—increased the risk of miscarriage by 2.4 times compared to abstaining from the medication.

1.3.6 Adverse Effects

Gastrointestinal Irritation: Ibuprofen may cause symptoms such as heartburn, nausea, vomiting, and indigestion by irritating the lining of the stomach. Severe instances may result in bleeding and stomach ulcers. The drug increases the risk of severe bleeding in the gastrointestinal tract, especially in older individuals, those with a history of ulcers, and anyone taking corticosteroids or blood thinners at the same time.

Renal Impairment: Excessive or prolonged use of ibuprofen may damage the kidneys, particularly in those who already have renal problems or are dehydrated. This can lead to kidney failure or damage.

Fluid Retention and Swelling: Because ibuprofen affects renal function and electrolyte balance, it might result in fluid retention and edema, especially in the lower limbs.

Cardiovascular Concerns: Using ibuprofen for an extended period of time or at high doses may increase the risk of strokes or heart attacks. It may cause blood pressure to rise and interfere with platelet activity, which is essential for blood coagulation.

Allergic Reactions: Ibuprofen allergies may range in severity from minor rashes to severe anaphylaxis, which is marked by swelling, a decrease in blood pressure, and difficulty in breathing.

Hepatic Toxicity: Although uncommon, high ibuprofen consumption may cause liver damage or failure, especially in those with underlying liver diseases or when used in combination with other drugs that strain the liver.

Effects on the Nervous System: Ibuprofen may cause headaches, vertigo, and in rare instances, anxiety or disorientation. Extended use may also be a factor in mood disorders or depression

Asthma Exacerbation: Taking ibuprofen may cause asthma episodes or worsening symptoms in those with aspirin-sensitive asthma.

1.3.7 Drug Interactions

Drug-Drug Interactions:

Drug Class	Interacting Drug	Potential Interaction
Anticoagulants	Warfarin, Heparin	Increased risk of bleeding due to antiplatelet effects of ibuprofen.
Antiplatelet Agents	Aspirin, Clopidogrel	Increased risk of bleeding due to additive antiplatelet effects.
Corticosteroids	Prednisone, Dexamethasone	Increased risk of gastrointestinal ulcers and bleeding.
Selective Serotonin Reuptake Inhibitors (SSRIs)	Fluoxetine, Sertraline	Increased risk of gastrointestinal bleeding due to inhibition of platelet function.
Angiotensin-Converting Enzyme (ACE) Inhibitors	Lisinopril, Enalapril	Decreased effectiveness of ACE inhibitors, leading to reduced blood pressure control.
Diuretics	Furosemide, Hydrochlorothiazide	Decreased effectiveness of diuretics, leading to reduced diuretic effect and potential fluid retention.
Antimanics	Lithium Carbonate	Increased lithium levels in the blood, leading to toxicity.
Antimetabolites	Methotrexate	Increased risk of methotrexate toxicity due to reduced renal clearance.
Antihypertensives	Amlodipine, Metoprolol	Decreased effectiveness of antihypertensive medications, leading to elevated blood pressure.
Immunosuppressants	Cyclosporine	Increased risk of kidney damage and nephrotoxicity. Monitor kidney function closely.

This table provides a brief overview of potential drug interactions with ibuprofen. It is essential to consult healthcare professionals for personalized advice and to review specific medication combinations.

Food-Drug interactions:

Food/Drink	Effect on Ibuprofen Absorption
Combination with Food	No significant effect on absorption.
Heavy Vegetarian Breakfast	Significantly increases the C_{max} and AUC_{0-48} of ibuprofen.
Coca-Cola	Significantly increases C_{max} and $AUC_{0-alpha}$ of ibuprofen.
Tamarindus Indica Fruit Extract	Significantly increases ibuprofen bioavailability.

1.3.8 Dosage regimen

- Ibuprofen 200–400 mg every 4-6 hours is the standard therapy for those between the ages of 20 and 45 who have a fever and mild pains.
- 300–800 mg of ibuprofen given three or four times a day is the standard dosage for treating arthritis sufferers.
- If someone has a fever for more than three days or discomfort for longer than ten days, it is recommended that they do not use ibuprofen unless a doctor gives them special instructions.
- Ibuprofen is usually given for fever and pain relief in children between the ages of six months and twelve years, with a daily maximum dose of no more than 40 mg/kg. The dosage should be administered no more often than every six to eight hours.
- Ibuprofen dosages ranging from 20 to 40 mg/kg/day, spread out across three to four doses over the day, are normally prescribed for patients with juvenile arthritis.

1.3.9 Overdose

Ibuprofen overdose can cause sudden kidney failure and seizures, which can affect the production and elimination of acidic compounds. Metabolic acidosis can cause: heart dysfunctions. changes

in blood pressure. Toxic effects are usually not seen at doses of less than 100 mg/kg but they can be severe when doses exceed 400 mg/kg.

An ibuprofen overdose has to be managed quickly by a medical professional. Following is a broad framework for handling an ibuprofen overdose:

Assessment and Stabilization: First, the patient's health needs to be assessed in detail, taking note of vital indicators such blood pressure, heart rate, breathing rate, and temperature. As needed, breathing, circulation, and airway is to be stabilized. The patient's neurological and mental health should be examined.

Decontamination: If the patient is at danger of serious toxicity and the ingestion happened within an hour, using activated charcoal may be taken into consideration. Ibuprofen's absorption into the circulation is lessened by activated charcoal.

Therapy for Symptoms: It is critical to treat symptoms including pain, nausea, and vomiting. If nausea and vomiting are continuous, antiemetics should be used.

Enhanced Elimination: To improve the clearance of ibuprofen from the bloodstream, hemodialysis may be taken into consideration in extreme instances or if the patient is at danger of major toxicity.

Monitoring and Follow-Up: It is important to keep a close eye on for any indications of escalating toxicity. Arrangements should be made for follow-up care to guarantee full healing and evaluate for any potential long-term issues.

With an emphasis on the importance and reasoning behind each action in reducing the negative impact of the overdose on the patient's health, this explanation offers a thorough rundown of the procedures involved in managing an ibuprofen overdose.

1.3.10 Ibuprofen Tablet Products Available in the Local Market

Ibuprofen is manufactured and marketed in various dosage forms including tablets, capsules, oral suspensions, and topical formulations. In tablet form, both conventional

and sustained-release formulations are available. Conventional tablet products typically come in various strengths ranging from 200 mg to 800 mg and are designed for immediate release of the medication upon ingestion. Examples of conventional tablet products include Advil, Motrin,Flamex and generic ibuprofen tablets.

Table 2 presents a list of Ibuprofen tablet products available in Bangladesh Pharma market:

Table 2: Trade name and respective companies of Ibuprofen

Brand Name	**Dosage Form**	**Strength**	**Manufacturer**
Advel	Tablet	400 mg	Opsonin Pharma Ltd.
Flamex	Tablet	400 mg	ACI Limited
Intaflam	Tablet	400 mg	Incepta Pharmaceuticals Ltd.
Profen	Tablet	400 mg	ACME Laboratories Ltd.
Reumafan	Tablet	400 mg	Beximco Pharmaceuticals Ltd.
Inflam	Tablet	400 mg	Synovia Pharma PLC
G-Ibuprofen	Tablet	400 mg	Gonoshasthaya Pharma Ltd.
Neurofen	Tablet	400 mg	Globe Pharmaceuticals Ltd.
Deflam	Tablet	400 mg	Desh Pharmaceuticals Ltd.
Serviprofen	Tablet	400 mg	SANDOZ (A Novartis Division)

Among the various brands given in the above table mainly two products, *viz.*, Advel and Flamex are in active supply.

1.4 Ailments and Disorders Treated by Ibuprofen

1.4.1 Pain

Pain is a complicated sensory and affective experience that is characterized by pain, suffering, and physical discomfort and is usually linked to actual or prospective tissue damage. It acts as a vital warning signal in the body, informing us of impending danger and causing us to take preventative measures.

Pain can be classified into two categories:

- **Acute pain:** Acute pain is a brief, intense suffering that strikes unexpectedly and is often caused by an accident or sickness. It alerts the body to impending danger. Usually, it goes away as the underlying cause gets better.
- **Chronic pain:** Chronic pain endures for an extended duration, frequently surpassing the anticipated healing period. It can be attributed to conditions like arthritis, neuropathy, or fibromyalgia, and has a substantial impact on daily activities and well-being.

Pain killer: The purpose of painkillers, also referred to as analgesics, is to reduce or control pain. Their mechanism of action involves hindering the body's ability to transmit pain signals, which lowers the sense of discomfort experienced. Nonsteroidal anti-inflammatory medicines (NSAIDs), *e.g.*, ibuprofen and acetaminophen, opioids, and other pharmaceuticals are some of the several categories into which painkillers may be divided. As useful as they are in relieving pain, painkillers should only be used sparingly and under a doctor's supervision to prevent reliance and any negative consequences.

1.4.2 Common cold:

The common cold is a contagious respiratory illness that is mostly caused by rhinoviruses. Symptoms include congestion, sneezing, coughing, headaches, and minor body pains. Daily living may be disrupted, even though it is typically not severe. Recuperation with rest, fluids, and over-the-counter medications usually takes a week to ten days. Hand cleaning, covering the mouth and nose while sneezing or coughing, and avoiding direct contact with the sick are preventive practices. Ibuprofen and other NSAIDs (Non-Steroidal Anti-Inflammatory Drugs) are commonly used to alleviate symptoms of the common cold such as fever and body aches. They help reduce inflammation and discomfort, providing relief during the illness. However, they do not directly

treat the underlying viral infection causing the cold. It's important to use them cautiously and according to recommended doses to avoid potential side effects.

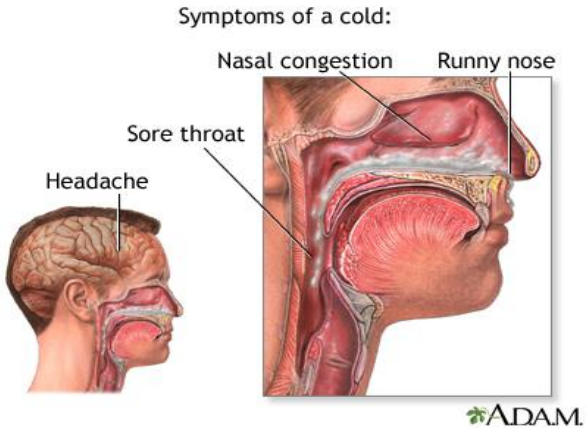


Figure 1.5:Common cold

1.4.3 Flu

Influenza, often referred to as 'the flu', is caused by a common respiratory virus that is very infectious. It differs from the ordinary cold. The flu virus is readily transmitted by humans and may cause moderate to severe disease, as well as death, in small children, elderly adults, and susceptible persons of all ages. Sneezing, coughing, or touching your mouth or nose after coming into contact with infected surfaces. There are two common forms of flu that sicken people: A and B. These viruses are known as seasonal flu viruses because they often appear in the winter. The trivalent influenza A vaccination include three strains of the virus. The quadrivalent vaccination introduced later includes influenza B as well. Ibuprofen and other NSAIDs (Nonsteroidal Anti-Inflammatory Drugs) can help relieve symptoms of flu, such as fever and body aches, by reducing inflammation and pain. However, they should be used with caution due to potential side effects and interactions with other medications. Always consult a healthcare professional for proper guidance.

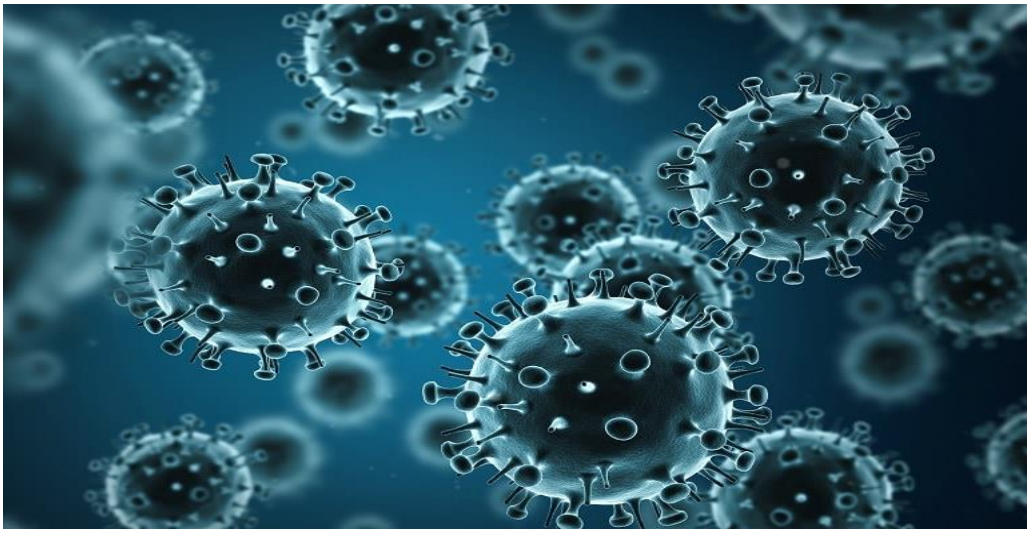


Figure 1.6: Flu

1.4.4 Headache

A frequent problem, headaches have a complicated pharmacology that stems from the anatomy and physiology of the tissues that cause pain. Migraine provides a paradigm for comprehending the activation, mediation, and modulation of nociceptive systems in the brain by neurotransmitters. The significance of serotonin (5-HT) in headache pharmacology has been clarified by recent research, especially its connection to nociceptive systems and its potential for treatment via 5-HT1 receptor subtypes. The framework of trigeminovascular nociception anatomy and physiology is used to examine the pharmacology of head pain systems, their development, and clinical issues such as efficacy, recurrence, and adverse events. Ibuprofen and other NSAIDs are crucial for treating headaches by reducing pain, inflammation, and fever through inhibiting prostaglandin production. They address headache causes like muscle tension, inflammation, or blood vessel dilation. Ibuprofen is popular due to its potency and lower risk of side effects with proper use. However, NSAIDs should be used cautiously due to potential gastrointestinal irritation and other adverse effects, especially with long-term or high-dose use. Seeking medical advice for diagnosis and treatment is advisable.

1.4.5 Dental Pain

Dental pain, which may also be referred to as odontalgia or toothache, is any soreness or discomfort that originates in the surrounding tissues or teeth. Tooth decay, gum disease, oral trauma, infection, or tooth sensitivity are just a few of the possible reasons. Dental pain may impair speech, eating, and general quality of life. It can also vary from moderate discomfort to severe, incapacitating agony. To relieve tooth pain, cure its underlying cause and avoid further issues, a dentist must diagnose and treat patients as soon as possible. Ibuprofen and other NSAIDs (Non-Steroidal Anti-Inflammatory Drugs) are commonly used in the treatment of dental pain due to their potent anti-inflammatory and analgesic properties. They help reduce pain, inflammation, and swelling associated with dental conditions such as toothaches, dental abscesses, and post-operative discomfort.

1.4.6 Patent Ductus Arteriosus (PDA):

The pulmonary artery and the descending aorta are connected by the patent ductus arteriosus (PDA), a fetal vascular opening that usually closes soon after birth. Yet, depending on its size and the person's cardiovascular condition, its continuation during the newborn stage may result in varied degrees of clinical relevance. Regardless of size, problems may occur, thus cardiologists treating juvenile and adult patients alike need to have a solid grasp of the pathogenesis, clinical consequences, and therapy of PDA. Ibuprofen and other NSAIDs (non-steroidal anti-inflammatory drugs) are used in the treatment of Patent Ductus Arteriosus (PDA) to induce closure of the ductus arteriosus, a vital connection between the aorta and pulmonary artery in fetuses that typically closes shortly after birth. These drugs help by inhibiting the production of prostaglandins, which are necessary for keeping the ductus arteriosus open. By promoting closure, NSAIDs aid in resolving PDA and preventing associated complications such as heart failure.

1.4.7 Gout (Inflammatory Arthritis)

The body's response to urate overload-induced urate crystal buildup in joints is gout arthritis. It has been connected to a number of comorbid conditions, including obesity, diabetes, cardiovascular disease, and chronic renal disease. In order to manage it, one must focus on lowering inflammation and urate levels to less than 0.36 mmol/L. Because patients often have poor

drug adherence, patient education on lifetime therapy and prophylaxis is essential, even with the advent of urate-lowering therapies.NSAIDs like ibuprofen are commonly used in the treatment of acute gout attacks to relieve pain and reduce inflammation. They work by inhibiting the production of prostaglandins, which are chemicals that contribute to inflammation. However, caution is advised in patients with kidney disease or gastrointestinal issues, and NSAIDs should be used at the lowest effective dose for the shortest duration possible to minimize side effects.

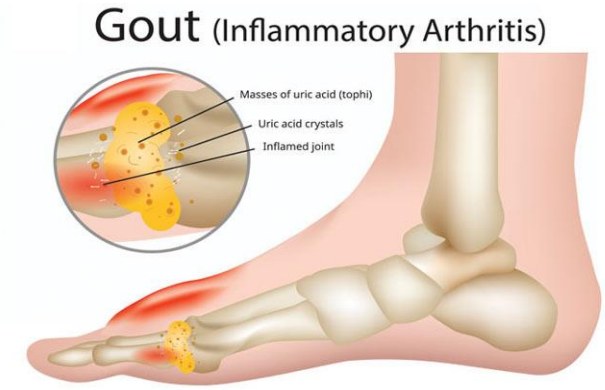


Figure 1.7: Gout (Inflammatory Arthritis)

1.4.8 Rheumatoid arthritis

Rheumatoid arthritis (RA) is an inflammatory illness that mostly affects the joints and is characterized by inflammation, stiffness, swelling, and pain. Neglecting it might lead to irregularities and joint damage. Rheumatoid arthritis (RA) develops when the immune system mistakenly targets the body's own tissues, namely the synovium. The exact cause is unknown, although genetic and environmental factors have a role. Relieving pain, reducing inflammation, and preventing joint injuries are the objectives of therapy. The following are sometimes employed: medication, physical therapy, dietary changes, and surgery. Early identification and intervention are critical to the effective treatment of RA and the improvement of the quality of life for those affected by the condition.Ibuprofen and other NSAIDs (Nonsteroidal Anti-Inflammatory Drugs) play a role in managing the symptoms of rheumatoid arthritis by reducing inflammation and relieving pain. However, they do not address the underlying causes of the disease or prevent its progression. They are typically used as part of a comprehensive treatment plan that may also include disease-modifying antirheumatic drugs (DMARDs) and biologic therapies.

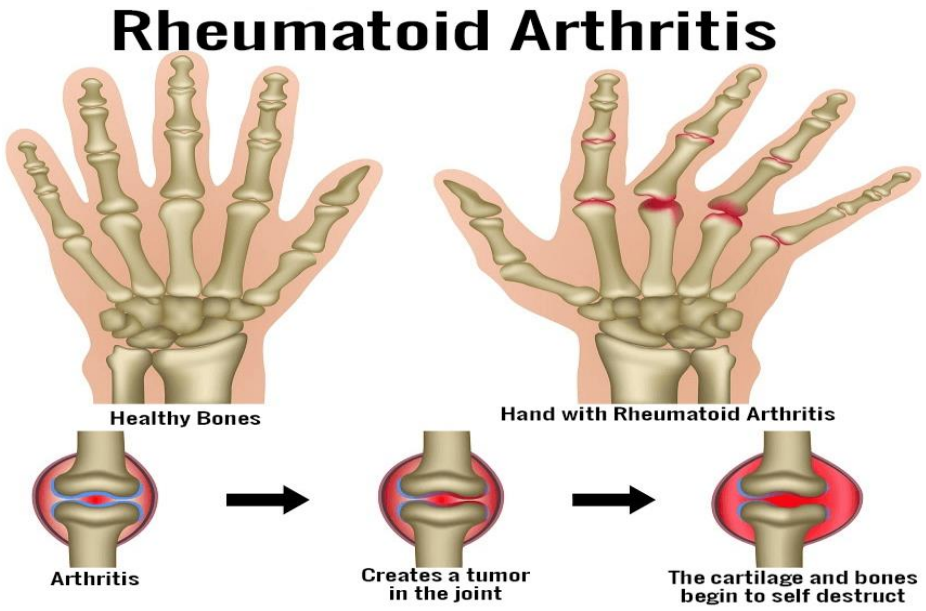


Figure 1.8: Rheumatoid Arthritis

1.4.9 Osteoarthritis:

Degenerative joint disease called osteoarthritis is defined by the deterioration of joint cartilage, which causes pain, stiffness, and reduced movement. Weight-bearing joints including the spine, hips, and knees are often impacted. Genetics, age, obesity, and joint damage are risk factors. Physical therapy, lifestyle changes, pain treatment, and in extreme situations, surgery are all part of the management process. Improving quality of life and reducing symptoms may be achieved with early diagnosis and treatment.Ibuprofen and other NSAIDs (Non-Steroidal Anti-Inflammatory Drugs) are commonly used to manage symptoms of osteoarthritis. They work by reducing inflammation and relieving pain. However, long-term use may have adverse effects on the gastrointestinal tract and kidneys. Therefore, their use should be carefully monitored and balanced with potential risks, especially in patients with pre-existing conditions.

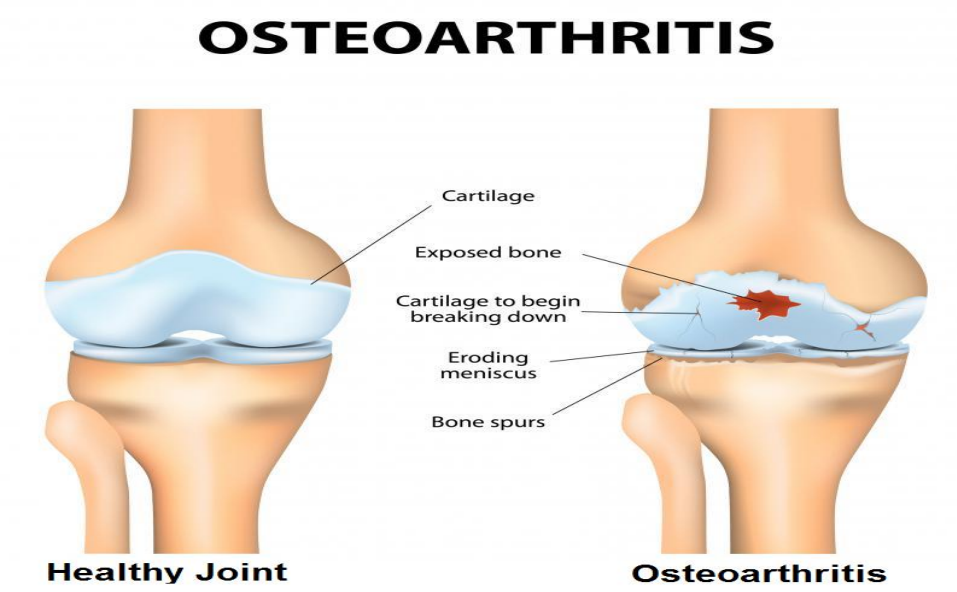


Figure 1.9: Osteoarthritis

1.4.10 Fever

The presence of compounds called pyrogens may induce fever, which is a clinical indicator of the body's reaction, often to microbial diseases. These pyrogens may be classified as endogenous, meaning they are created within the body, like interleukin and interferon, or exogenous, meaning they come from outside sources like infections. In fever caused by infections tissue damage may occur if microbial invasion goes uncontrolled. White blood cells are drawn to the infection site by chemotaxis, which is caused by the production of inflammatory mediators such as histamine, kinins, prostaglandins, leukotrienes, and interleukins. Among these cells, macrophages are essential because they consume pathogens via phagocytosis and trigger the production of cytokines to boost the immune system. Macrophages, sometimes referred to as monocytes, make up a substantial fraction of the cells found in different organs.Ibuprofen and other NSAIDs (nonsteroidal anti-inflammatory drugs) are commonly used to reduce fever. They work by inhibiting the production of prostaglandins, which are substances in the body that cause inflammation and fever. By blocking prostaglandin production, NSAIDs help to lower body temperature and relieve fever.

1.4.11 Dysmenorrhea

People who suffer from dysmenorrhea frequently have painful menstruation, which is accompanied by symptoms including nausea, vomiting, and exhaustion. The discomfort is usually felt in the lower abdomen. When there is no underlying medical condition causing the dysmenorrhea, heat treatment, over-the-counter pain relievers, and lifestyle modifications are often used to relieve it. Secondary dysmenorrhea, on the other hand, which is linked to diseases like endometriosis or uterine fibroids, requires therapy that targets the underlying cause.Ibuprofen and other NSAIDs (Nonsteroidal Anti-Inflammatory Drugs) are commonly used to relieve dysmenorrhea, or menstrual pain. They work by inhibiting prostaglandin synthesis, which reduces uterine contractions and inflammation, thus alleviating pain.

Chapter Two: Materials and Methods

2.1 Materials and Reagents

Materials

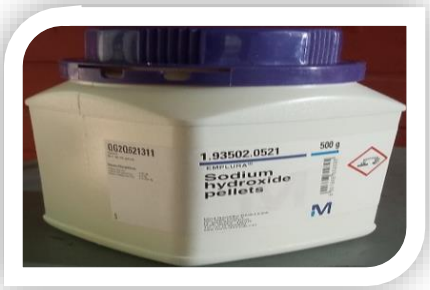
- **Active Pharmaceutical Ingredient (API):** Ibuprofen (potency-99.7%; impurity-0.20%; LOD-0.50%; white fine crystalline powder)
- **Tablet/Finished Product:** Two brands of conventional Ibuprofen Tablets (400 mg)

Reagents and Solvents

Table 2.1 lists the reagents and solvents used in the work:

Table 2.1: Reagents and Solvents

Name	Source	Country of origin
Sodium hydroxide	Merck	Germany
Distilled water	Pharmaceutics Laboratory, Department of Pharmacy, Jahangirnagar University	Bangladesh
Dibasic potassium phosphate	Merck	India
Monobasic potassium phosphate	Merck	India
Alcohol	Merck	Germany



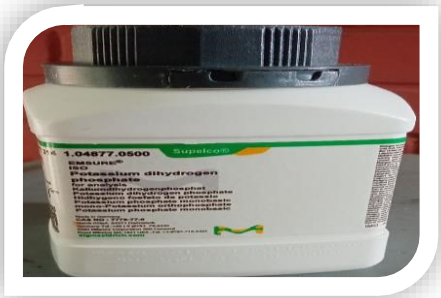



Figure 2.1: Reagents & solvents

Glassware and Other Accessories

Table 2.2 lists the apparatus and glassware used in the work.

Table 2.2: Apparatus and Glassware

Name	Specifications
Volumetric flask	50 ml, 100 ml, 500 ml & 1000 ml
Measuring cylinder	10 ml & 50 ml
Pipette	10 ml
Funnel	Small & Medium
Test tubes and test tube racks (steel, plastic & wooden)	Small & Medium
Beaker	50 ml, 100 ml, 250 ml, 500 ml, 800 ml & 1000 ml
Spatula	Small
Stirrer/ Glass rod	Small
Pipette filler	Small
Mortar & Pestle	Medium
Aluminum foil	Standard
Filter paper (Double rings)	11.0 cm
Kim wipes (Kimtech)	11cm x 21cm
Falcon tube	15 ml
Dropper	Small
Conical flask	250 ml, 1000 ml & 2000 ml
Distilled water dispenser	250 ml & 500 ml

Fig 2.2: Apparatus and Glassware

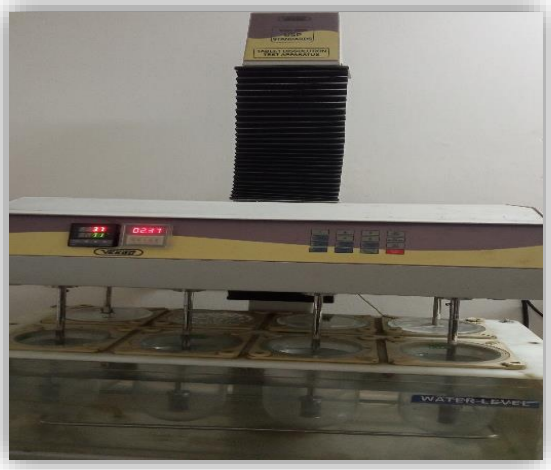
Equipment and Instruments

Table 2.3 lists the equipment and instruments used in the study with their models/manufacturer names:

Table 2.3: Equipment and Instruments

Instruments	Model/Manufacturer	Purpose
 **UV-Vis Spectrophotometer**	UV 1601 PC SHIMADZU Japan	To study the release pattern and potency of the tablet
 **Electronic Balance**	AND-GULF Precision Electronic Balance China	For precise measurement of various ingredients
	Gallenkamp UK	For drying up the glassware

Hot Air Oven		

Instruments	Model/Manufacturer	Purpose
 **pH Meter**	SI analytics lab 845 Germany	For the measurement of pH of the prepared release media
 **Dissolution Tester**	Veego India	To study the release profile of tablets

Slide Calipers	SDK China	To measure the thickness & diameter of tablets
 **Hardness Tester**	Campbell Electronics India	To measure the hardness of tablets

Instruments	**Model/Manufacturer**	**Purpose**
 **Friability Testing Apparatus**	Campbell Electronics Bombay 400025 Thermonik, India	To measure the friability of tablets
 **Disintegration Test machine**	Campbell Electronics Bombay 400025 Thermonik, India	To measure the disintegration time of tablets

 **Magnetic heating Stirrer**	CJJ78-1 Magnetic Heating Stirrer China	For thorough mixing

Instruments	Model/Manufacturer	Purpose
 **Centrifuge Machine**	TDL-60B Human Lab Instrument Co, Korea	For the separation of insoluble solid particles from a liquid sample

2.2 Methods

2.2.1 Collection of samples

- **Active Pharmaceutical Ingredient (API): Ibuprofen** (API) was a kind gift donated by ACI Pharmaceuticals Ltd., Bangladesh.
- **Tablet samples:** Two brands of Ibuprofen Conventional Tablets of 400 gm strength available locally were collected from different retail pharmacies located in Savar and Dhaka area and were coded as **A-400** and **F-400**. It may be noted here that many other pharmaceuticals have taken formal approval to manufacture the product, but their products are not in active supply.

2.2.2 Assessment of physical parameters

The tablet products were assessed for the following physical parameters:

- Organoleptic properties
- Thickness and diameter
- Hardness & Friability
- Weight and weight variation
- Disintegration time

2.2.2.1 Organoleptic properties: We looked at and noted the tablet items' color and odor.

2.2.2.2 Thickness and diameter: Ten tablets were randomly selected from each group and, using the slide calipers, their thickness and diameter were measured in millimeters.

2.2.2.3 Hardness test: Five tablets were chosen from each group and their hardness was measured using Monsanto Hardness Tester (Campbell Electronics, India). The test tablet was positioned diametrically between the fixed and moving jaws, and the indicator's reading was set at zero. After that, force was applied until the tablet cracked. The force required to just cause the tablet carack was recorded in kg/cm^2.

2.2.2.4 Friability test: For testing 10 tablets were taken randomly and placed on a sieve. Loose dust was removed with the aid of air pressure or a soft brush. Tablet samples were weighed accurately and placed in the fiabilitor. After revolving the instrument for the given number of rotations (100 rotations/4 min) loose dust was removed from the tablets as before and the tablet samples were re-weighed.

The friability (% loss in weight) of the tablet products was determined using the following formula:

$$\% \text{ Friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

2.2.2.5 Weight and weight variation

- From each group ten tablets were taken at random and weighed. The average weight was calculated.
- Then each tablet was weighed individually, and their weights were compared with the average weight.
- The maximum upper and lower weight variation (%) were calculated using the following formula:

$$\textbf{Maximum upper weight variation} = \frac{\textbf{Highest weight} - \textbf{Average weight}}{\textbf{Average weight}} \textbf{ x 100}$$

$$\textbf{Maximum lower weight variation} = \frac{\textbf{Average weight} - \textbf{Lowest weight}}{\textbf{Average weight}} \textbf{ x 100}$$

2.2.3 Disintegration test

A USP disintegration tester (Campbell Electronics Bombay 400025 Thermonik, India) was used to determine the disintegration times of six tablets per brand in distilled water at 37.0 ± 0.5 C. The device consists of a group of tubes that are opened at the top and covered with a No. 10 mesh screen with a diameter of 2 mm at the bottom. One tablet was placed in each tube. The entire assembly was then submerged in 900 milliliters of distilled water in a 1-liter beaker. A consistent

temperature of 37.0 ± 0.5 C was maintained in the beaker by placing it within the water bath. The basket (assembly) holding the tablets was moved up and down at a distance of 5–6 cm at a frequency of 28–32 cycles per minute using a typical motor-driven device. The disintegration time was defined as the amount of time needed for each of the six tablets to split up into granules large enough to go past the mesh.

2.2.3.1 Preparation of media for disintegration test: The test was carried out in two different media:

a. Distilled water

b. Simulated gastric fluid (pH 1.2)

2.2.3.1.1 Distilled water: Distilled water was prepared in the Pharmaceutics Laboratory of Pharmacy Department, JU using a Distillation Machine.

2.2.3.1.2 Preparation of simulated gastric fluid (pH 1.2): With the use of a pH meter, the pH was determined in order to produce simulated stomach fluid with 1.2 pH.

A final amount of 1000 ml was obtained by diluting 8.36 ml of 37% concentrated hydrochloric acid (HCl) with water.

A pH meter was used to continuously monitor the pH and make necessary pH changes using either HCl or NaOH.

2.2.4 Assay

The assay of Ibuprofen Tablet products was performed spectrophotometrically by a UV-Vis Spectrophotometer (UV 1601 PC, SHIMADZU, Japan). The assay was carried out using 0.1N NaOH as the solvent.

2.2.4.1 Preparation of 0.1N Sodium Hydroxide (NaOH) Solution: 0.1N sodium hydroxide (NaOH) solution was prepared by dissolving 4g of NaOH in 1L of distilled water using a volumetric flask.

The pH of the prepared solution was adjusted to 13 by adding to it 1N sodium hydroxide dropwise.

2.2.4.2 Determination of the λmax of ibuprofen in 0.1N NaOH

To determine the the λ_{max} of ibuprofen in 0.1N NaOH, standard solutions of the drug prepared in the solvent system were scanned across a wavelength range of 200-400 nm by a UV-Vis Spectrophotometer (UV 1601 PC, SHIMADZU, Japan) using the same as the blank.

2.2.4.3 Preparation of ibuprofen stock solution: To prepare a stock solution of Ibuprofen in 0.1N NaOH (0.5 mg/ml) 50 mg of Ibuprofen (API) was accurately weighed and taken in a 100 ml volumetric flask. About 100 ml of 0.1 N NaOH was added and shaken to dissolve the drug in the volumetric flask containing the ibuprofen. Finally the volume was adjusted to 100 ml mark by adding required more of 0.1 N NaOH.

2.2.4.4 Preparation of standard calibration curve: In order to analyze the potency of the tablet samples, a standard calibration curve was prepared in 0.1N NaOH. A series of solutions of ibuprofen at different concentrations, *viz*., 1, 5, 10, 15, 20, 25, 30, 35 and 40 µg/ml, were prepared from the stock solution by appropriate dilution. Then using 0.1N NaOH as the blank, absorbances of the prepared solutions were measured at 226 nm. To construct the curve, absorbances were plotted against their respective concentrations using MS Excel program and the range of concentrations showing linear relationship giving a straight line was determined.

2.2.4.5 Preparation of ibuprofen sample solution:

- Twenty tablets from each brand were randomly selected and their weights were measured before being finely powdered.
- A precise amount of the powdered sample, equivalent to 100 mg of ibuprofen, was transferred into a 100 mL volumetric flask.
- Approximately 100 ml of 0.1 N NaOH was added to the flask containing the powdered ibuprofen and shaken thoroughly to dissolve it.

- The solution was further agitated using a Magnetic Heating Stirrer for a duration of 15 minutes.
- Undissolved materials were separated by centrifugation at 5000 rpm for 5 minutes.
- The supernatant was diluted sufficiently to give a solution having a concentration of approximately 15 µg/ml.

2.2.4.6 Determination of the potency of Ibuprofen Tablet by UV spectrophotometry

The absorbance of the prepared sample solution (of approximately 15 µg/ml) was measured by UV-Vis spectrometry at 226 nm using 0.1N NaOH as the blank and the actual concentration was determined from the standard curve equation.

The potency of the drug in the test sample is expressed as a percentage of the labeled or expected potency. This is calculated by comparing the measured concentration of ibuprofen in the test sample to the expected concentration in the same as per the label claim of the drug.

Following formula was used for calculating potency (% of the labeled amount) of the drug:

$$\textbf{Potency (\%)} = \frac{\mathbf{C1}}{\mathbf{C}} \textbf{ x 100}$$

where,

Expected concentration of the drug in the sample solution = C

Measured concentration of the drug in the sample solution = C_1

2.2.5 Dissolution study

2.2.5.1 Determination of the λmax of ibuprofen in phosphate buffer (pH7.2)

To determine the λmax of ibuprofen in phosphate buffer solution (pH 7.2), the absorbance of standard solutions of the drug in the solvent system was measured across a wavelength range, typically from 200 nm to 400 nm, using the same as the blank and the wavelength exhibiting the highest absorbance was identified. This value was used for subsequent analyses of ibuprofen.

2.2.5.2 Preparation of standard calibration curve

In order to analyze ibuprofen in the release medium, phosphate buffer solution (pH 7.2), a standard calibration curve was constructed from a series of standard solutions of the drug at different concentrations. Using the fresh media as the blank, absorbances of ibuprofen solutions at concentrations 1, 5, 10, 15, 20 and 25 in phosphate buffer solution (pH 7.2) were measured at the λmax of 222 nm. The curve was constructed by plotting the absorbances against the respective concentrations. The equation for the curve and the coefficient of determination (r2) was determined using the MS Excel program.

2.2.5.3 Dissolution study of ibuprofen tablet samples

The USP Apparatus 2 (Paddle Apparatus-Veego, India) was used to conduct the dissolution study on the collected ibuprofen tablet products using phosphate buffer (pH 7.2) as the release media. The device has 6 stations, each of which is composed of a motor, a transparent, inert material-covered vessel, and a metallic paddle shaft. The vessel has a 1000 ml nominal capacity and a cylindrical shape with a hemispherical bottom. Typically, one tablet is inserted into the vessel and stirred by the paddles attached to the motor-driven shaft. The paddle was submerged in the dissolution medium and the temperature was maintained at 37±0.5 °C using a constant temperature bath. The motor was set to rotate at 50 rpm, and 5 ml samples were taken out periodically for analysis at 0, 10, 20, 30, 45, 60, 90 and 120 min. An equal volume of fresh media was replaced immediately after withdrawing a sample to keep the total volume of media unchanged. To determine the cumulative amount of drug released at each interval, the absorbance of samples drawn was measured by UV-Vis spectrophotometer at 222 nm using phosphate buffer (pH 7.2) as the blank. The concentrations of the withdrawn samples were determined from the equation of a standard calibration curve constructed by plotting the absorbances, measured at 222 nm, of a series of standard ibuprofen solutions in phosphate buffer (pH 7.2) against their corresponding concentrations. Then the cumulative amount of drug released (%) at each time interval was calculated using the drug concentration of the withdrawn sample, the volume of the release media and label strength of the tablet product. The cumulative amounts of drug release (%) were plotted against the time intervals to graphically represent the drug release profile.

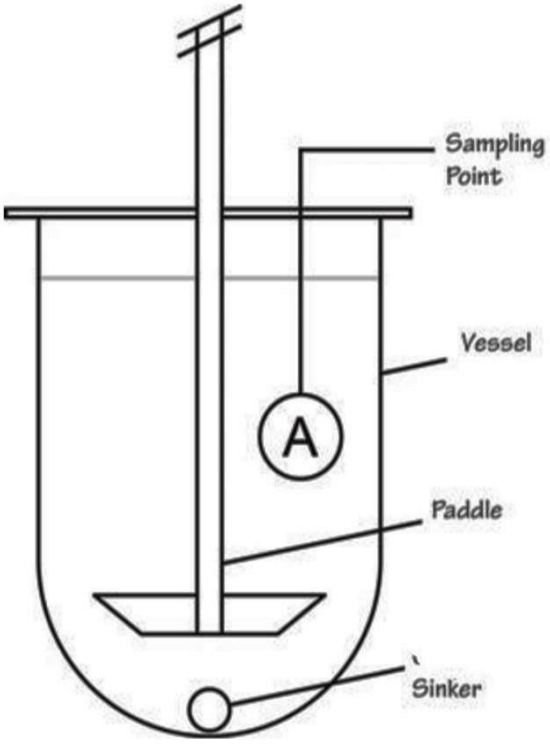


Figure 2.3: Dissolution apparatus

2.2.5.4 Dissolution conditions:

Apparatus: USP Apparatus 2 (Paddle Apparatus)

Medium: phosphate buffer solution (pH 7.2)

Volume: 900 ml

Speed: 50 rpm

Temperature: 37°C ± 0.5°C

Time: 2 hours

Intervals (min): 0, 10, 20, 30, 45,60, 90, 120

Chapter Three: Results

3.1 Physical parameters of tablets

3.1.1 Organoleptic properties

As shown in **Table 3.1** the tablet products were white in color. None of the tablet products, however, had any odor.

Table 3.1: Organoleptic properties of studied ibuprofen tablet products

Sample Code	Color	Odor
A-400	White	None
F-400	White	None

3.1.2 Shape, diameter and thickness

Shape: As shown in **Table 3.2**, both the tablet products (A-400 and F-400) were oblong in shape.

Table 3.2: Shapes of the studied tablet products

Sample Code	Shape
A-400	Oblong
F-400	Oblong

Diameter and thickness: Table 3.3 shows the average diameter and thickness of studied tablet products with maximum percentage of deviation from the average. The average diameter and thickness data are graphically illustrated in **Figures 3.1** and **3.2**, respectively. The average

diameters of the tablets were 15.8±.788 mm and 14.6±.394 mm for the products A-400 and F-400, respectively, while the average thicknesses were 6.1±0.738 mm and 4.74±0.400 mm, respectively.

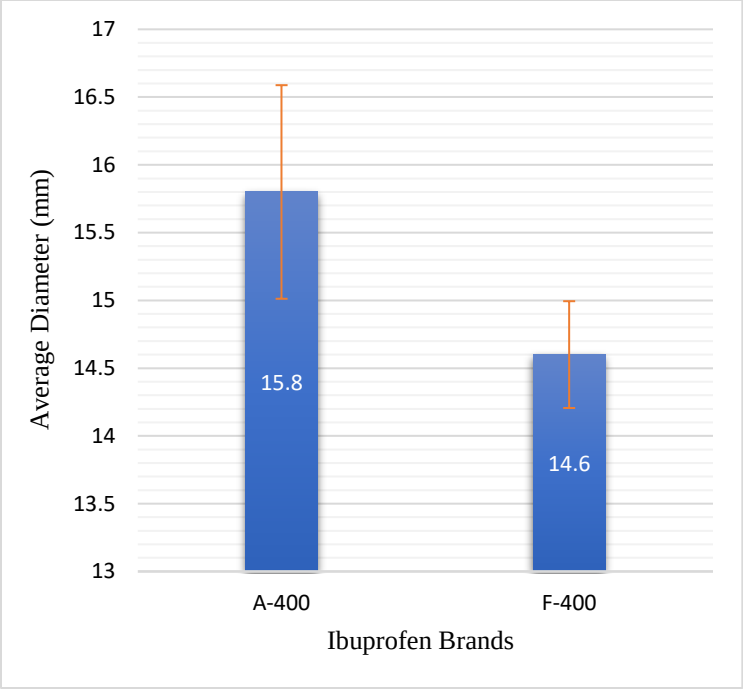


Figure 3.1: Average diameters of studied ibuprofen tablets

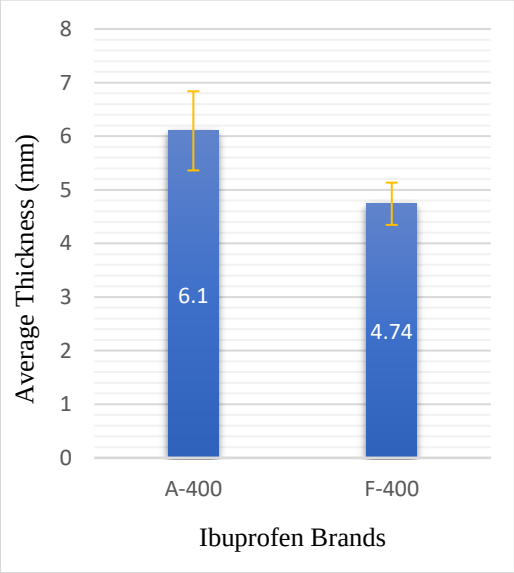


Figure 3.2: Average thickness of studied ibuprofen tablets

Table 3.3: Average diameter and thickness of tablet products with percentage (%) deviation from the average

Sample Code	Average Diameter ± S.D. (mm)	Maximum Deviation (%)	Average Thickness ±S.D. (mm)	Maximum Deviation (%)
A-400	15.8±0.788	7.595	6.1±0.738	18.033
F-400	14.6±0.394	4.110	4.74±0.400	15.612

3.2. Hardness test

Table 3.4 shows the individual and average hardness for 5 tablets of studied ibuprofen tablet products. The average hardness was found 3.28±0.074 kg/cm2 for A-400 and 9.8±0.234kg/cm2 for F-400. The data are graphically presented in **Figure 3.3.**

Table 3.4: Hardness of studied ibuprofen tablets

Sample Code	Tab-1	Tab-2	Tab-3	Tab-4	Tab-5	Average Hardness ± S.D. (kg/cm^2)
A-400	3.4	3.3	3.3	3.2	3.2	3.28±0.074
F-400	10	9.8	9.8	9.7	9.7	9.8±0.234

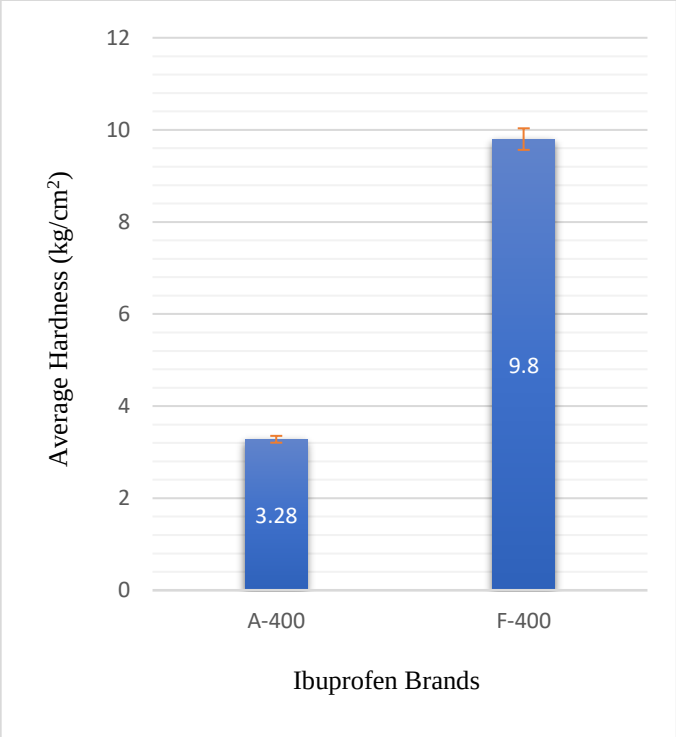


Figure 3.3: Average hardness of studied ibuprofen tablets

3.3 Friability test

The friability or percentage of loss of in the weight of the tablet products studied, after subjecting 10 randomly selected tablets from each brand to friability test, were found to be 0.215% for the product A-400 and 0.146% for the product (F-400) as shown in **Table 3.5** and graphically represented in **Figure 3.4**.

Table 3.5: Friability of the studied ibuprofen tablets

Sample code	Number of tablets	Initial weight (mg)	Final weight (mg)	Friability (%)
A-400	10	5557	5545	0.215
F-400	10	6134	6125	0.146

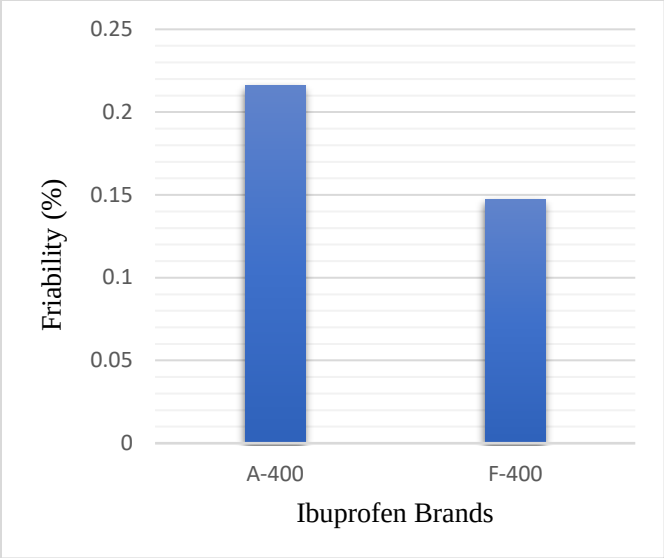


Figure 3.4: Friability of the studied ibuprofen tablets

3.4 Weight and weight variation test

Table 3.5 presents the average weights and maximum upper and lower weight variations for the tablet samples studied. The average weights of tablet products were 555.7±11.926 mg for A-400 and 613.4±6.257 mg for F-400. The maximum upper and lower weight variations were 2.573% & 3.185% for A-400, respectively. The corresponding values for F-400 were 1.728% and 1.532%, respectively. The data are graphically presented in **Figures 3.5 (a)** and **(b)**.

Table 3.6: Average weight and weight variation of studied ibuprofen tablets

Sample code	Average weight ± S.D. (mg)	Maximum Upper weight variation (%)	Maximum lower weight variation (%)
A-400	555.7±11.926	2.573	3.185
F-400	613.4±6.257	1.728	1.532

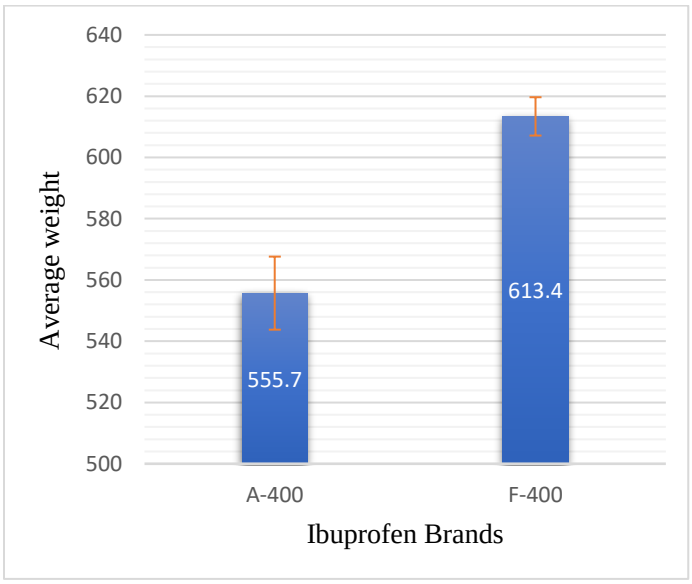


Figure 3.5 (a) Average weight and weight variation of studied ibuprofen tablets

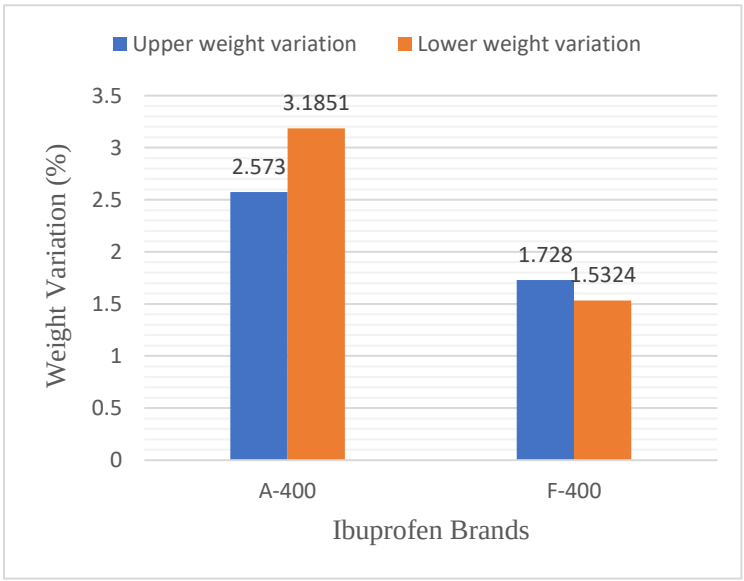


Figure 3.5 (b): Upper and lower weight variation of studied ibuprofen tablets

3.5 Disintegration test

Table 3.7 presents the disintegration times observed for the tablet products studied using 2 different media, *viz.*, water and simulated gastric fluid (0.1N HCl, pH 1.2). The data are graphically illustrated in **Figure 3.7.** The disintegration times in water were found 14 min in water and 14.5 min in simulated gastric fluid for the product A-400, while the corresponding values for F-400 were 2 min and 2.5 min, respectively.

Table 3.7: Disintegration times of studied tablet products

Sample code	Water (min)	Simulated gastric fluid (min)
A-400	14	14.5
F-400	2	2.5

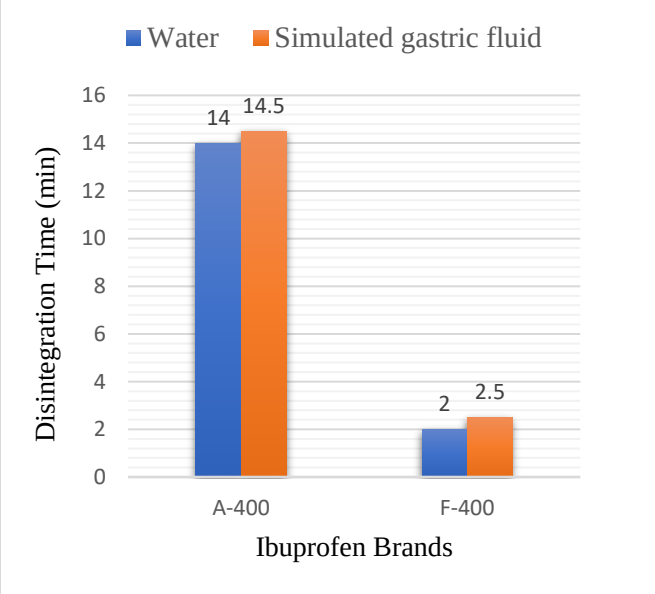


Figure 3.6: Disintegration times of studied tablet products

3.6 Assay

3.6.1 Determination of the λmax of ibuprofen in 0.1N NaOH: The λmax of ibuprofen in 0.1N NaOH was determined by scanning solutions of the drug in the same across a wavelength range of 200-400 nm and was found to be 226 nm. One spectrum of the drug in 0.1N NaOH at a concentration of 15 µg/ml is shown in **Figure 3.7**.

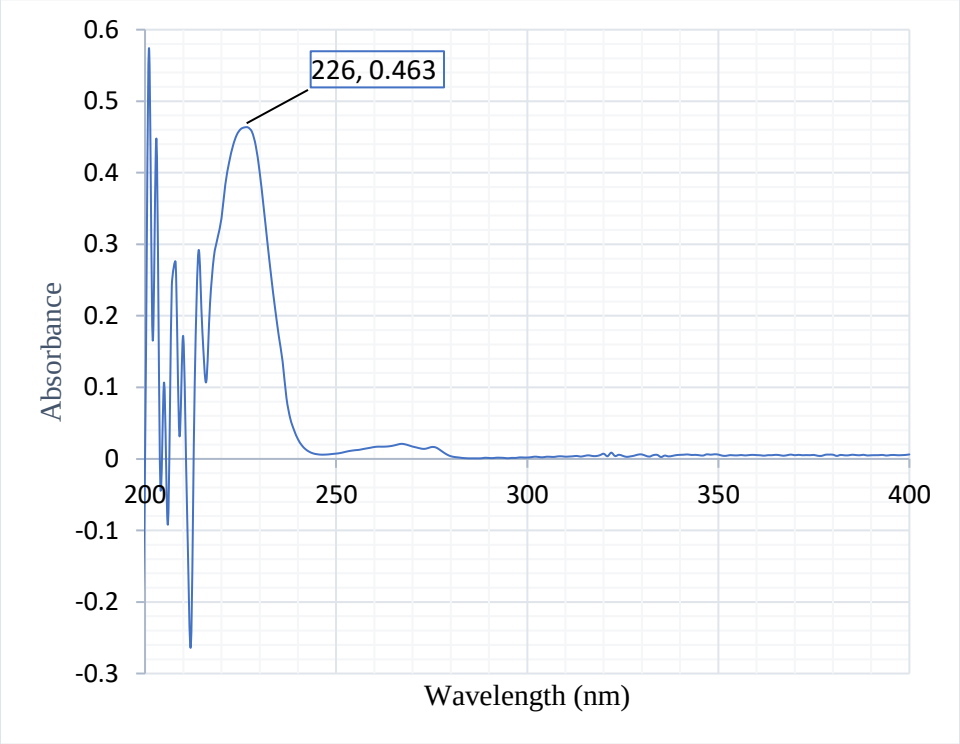


Figure 3.7: UV spectrum of ibuprofen in 0.1N NaOH

3.6.2 Construction of standard calibration curve of ibuprofen in 0.1N NaOH: Measurement of absorbance of ibuprofen solutions in 0.1N NaOH at different concentrations showed a linear relationship between the absorbance and concentration over a concentration range of 1 to 25 µg/ml giving a straight line with a coefficient of determination (r^2) of 0.9502 **(Table 3.8, Figure 3.8)**.

Table 3.8: Data for standard calibration curve of ibuprofen in 0.1N NaOH

Concentration (µg/ml)	5	10	15	20	25
Absorbance	0.035	0.283	0.455	0.983	1.039

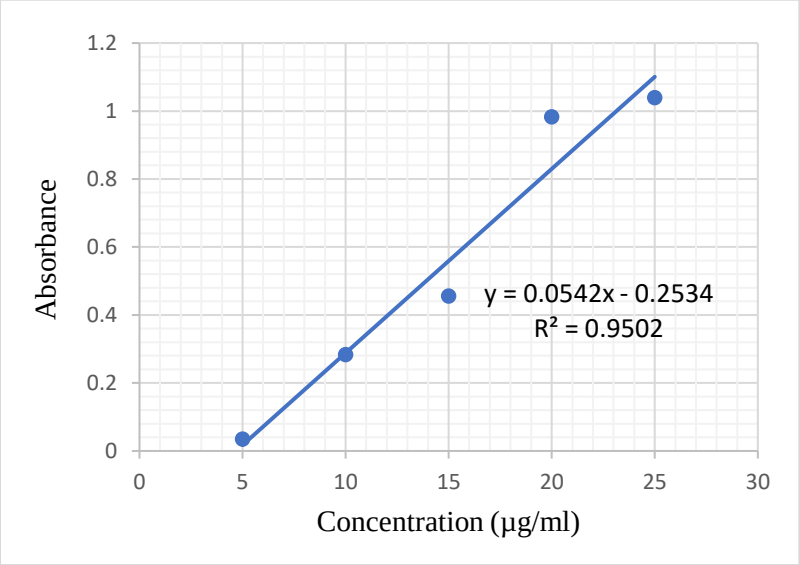


Figure 3.8: Standard calibration curve of ibuprofen in 0.1N NaOH

3.6.3 Determination of the potency of the tablet products:

Table 3.9 presents the assay results of studied ibuprofen tablet products using 0.1N NaOH as the solvent system. The data are graphically presented in **Figure 3.6**. Assay results demonstrate a potency of 98.450% for A-400 and 94.637% for F-400.

Table 3.9: Assay results of studied ibuprofen tablet products

Sample Code	Potency
A-400	98.450
F-400	94.637

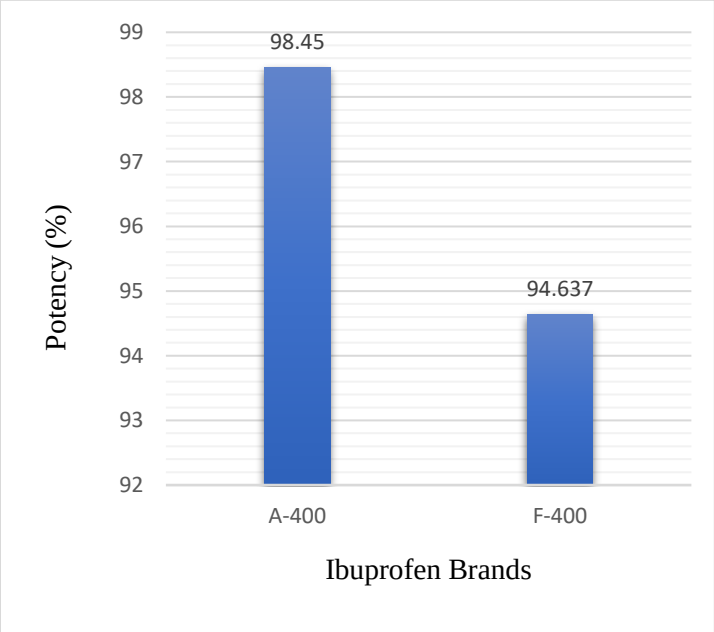


Figure 3.9: Assay results of studied ibuprofen tablets

3.7 Dissolution study

The dissolution study of ibuprofen tablets was performed by a USP Dissolution Testing Apparatus (Apparatus 2. Paddle) using phosphate buffer solution (pH 7.2) as the release media.

3.7.1 Determination of λmax of ibuprofen in phosphate buffer solution (pH 7.2)

As shown in **Figure 3.10**, upon scanning of ibuprofen solutions in phosphate buffer solutions (pH 7.2) by a UV-Vis spectrophotometer over a concentration range of 200-400 nm, the λmax of ibuprofen was found to be 222 nm.

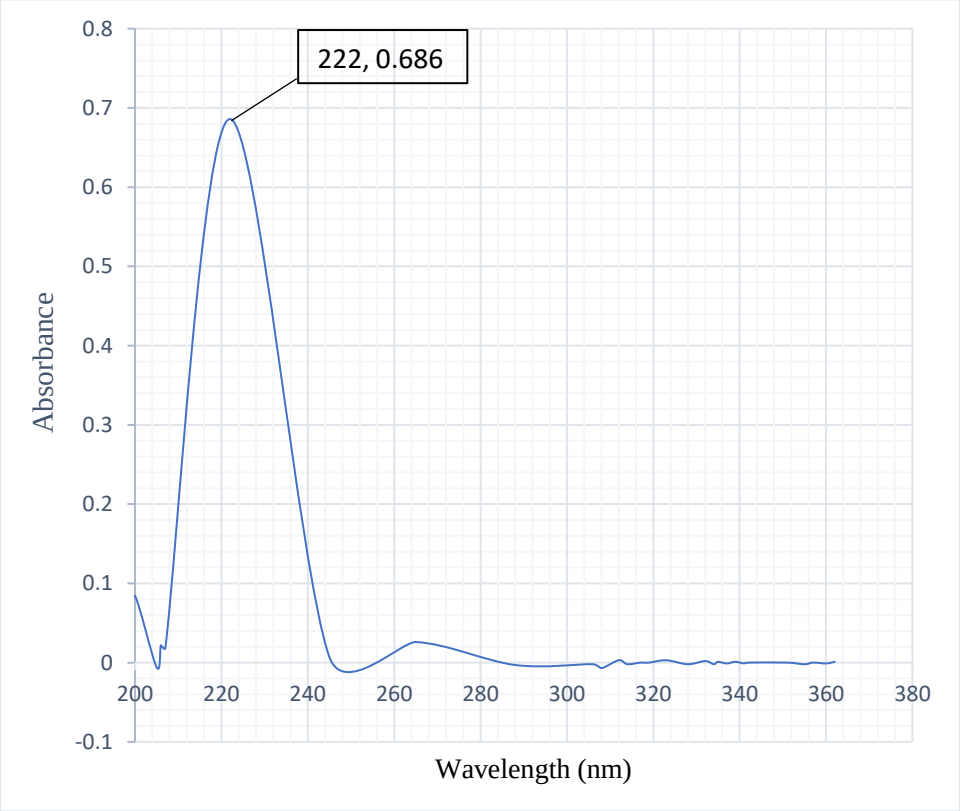


Figure 3.10: UV spectrum of ibuprofen in phosphate buffer (pH 7.2)

3.7.2 Construction of standard calibration curve of ibuprofen in phosphate buffer (pH 7.2)

Table 3.9 presents the data for standard calibration curves drawn for ibuprofen from standard solutions of the drug prepared in solvent systems, *viz.*, phosphate buffer (pH 7.2) at different concentrations. The curve drawn based on these data with the straight-line equation and coefficient of determination (r^2) values are shown in **Figure 3.11**.

Table 3.10: Data for standard calibration curves of ibuprofen in phosphate buffer (pH 7.2)

Concentration (µg/ml)	1	5	10	15	20	25
Absorbance	0.01	0.227	0.424	0.539	0.88	1.04

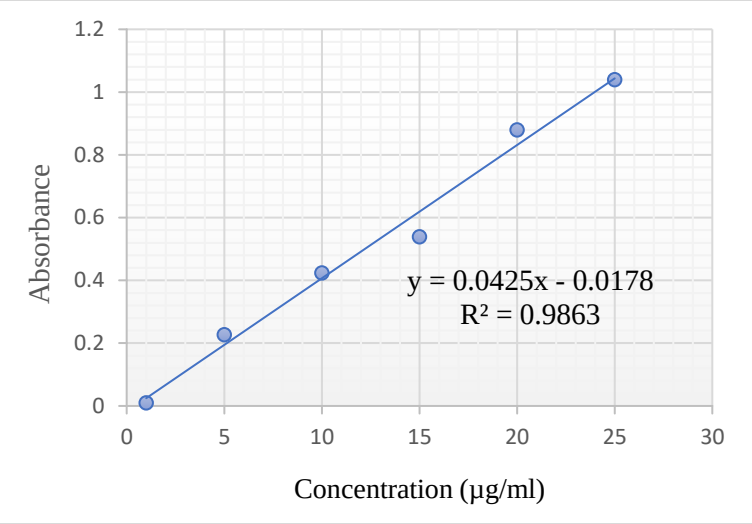


Figure 3.11: Standard calibration curve of ibuprofen in phosphate buffer (pH 7.2)

3.7.3 Dissolution study of ibuprofen tablet products

Table 3.11 presents the average % release from 6 tablets in phosphate buffer (pH 7.2) for each of the two brands of ibuprofen tablets studied. The data are graphically presented in **Figure 3.12**. As is evident from the results presented in **Table 3.11** and **Figure 3.12**, the release from the two brands was nearly identical and there was about 45%, 60% and 80% release at around 45, 60, 90 min time point. After the 90 min time point, there was not much increase in drug release.

Table 3.11: Release profiles of ibuprofen tablet samples in phosphate buffer (pH 7.2)

Sample Code	% of drug released (average of 6 tablets)							
	Time (min)							
	0	10	20	30	45	60	90	120
A-400	0	2.79	13.21	30.54	44.32	60.55	79.67	82.60
F-400	0	4.70	14.95	33.19	46.31	60.67	82.32	87.88

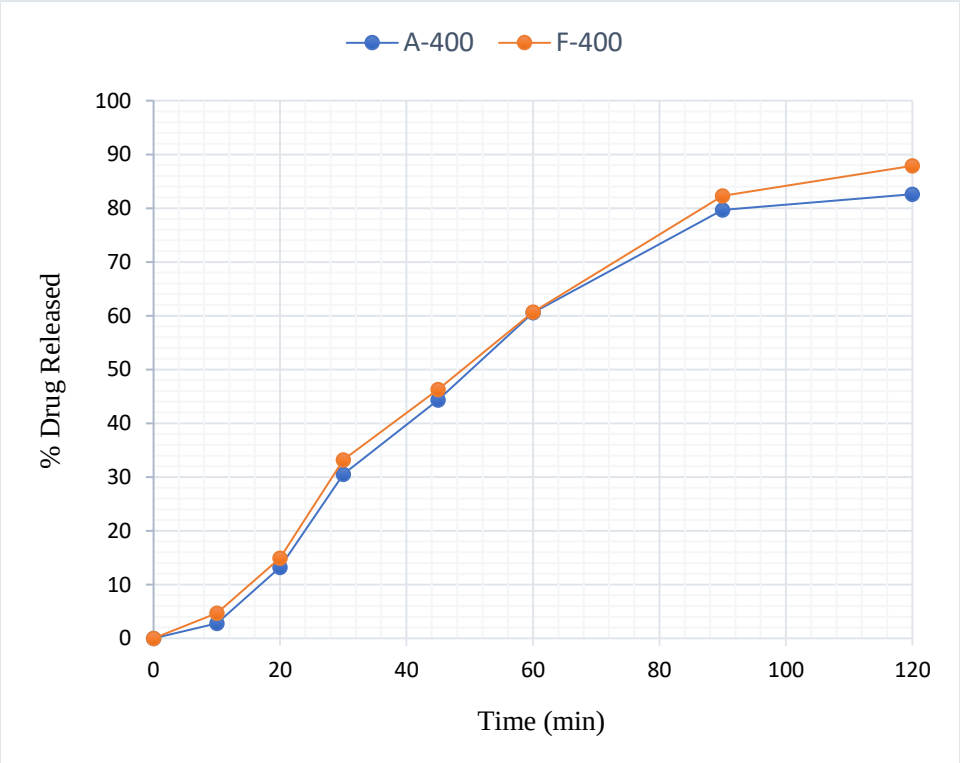


Figure 3.12: Release profiles of ibuprofen tablet samples in phosphate buffer (pH7.2)

Chapter Four: Discussion

In this study, two different brands of conventional ibuprofen tablets (400 mg) were collected from different retail pharmacies at Savar area of Dhaka district and then were subjected to a number of tests.

A comparative quality assessment is very important to evaluate tablet properties. Different comparative quality assessment parameters (e.g., weight and weight variation, thickness and diameter, hardness, assay of contents, friability, disintegration time and dissolution tests) were performed to determine the differences among various conventional ibuprofen tablets that are available in the Bangladesh drug market.

The pharmacopeial compliance with the weight uniformity of every brand under study is crucial since either weight variation or uniformity of content can be used to prove dosage unit uniformity. These either measure the quantity of drug material in the tablet directly or indirectly. Two different brands of ibuprofen tablets produced consistent weight determination results with values that are within acceptable bounds **(Table 3.6)**. Due to the varied excipients utilized in the two brands, there was a difference in their mean weight. The results of the weight uniformity test for both brands showed that their respective values corresponded with official criteria. Weight fluctuation is insufficient to ensure consistent efficacy of the tablets.

As stated on the product label, the potency of tablets is measured in milligrams, micrograms, or grams of medication per tablet. The variations in tablet weight, which reflect their sizes, between brands may have a negative psychological impact on clinicians and their patients even though the weight uniformity test was passed with each brand. This is because it may cast doubt on the general equivalency of the various brands of 400 mg ibuprofen tablets that are readily available.

The World Health Organization model formulary suggests that a patient be started on a certain brand for likely pharmacokinetic and psychological reasons. The amount of drug material in each

tablet unit should match the amount stated on the label. In order to assess content, an assay should be carried out. In order to ensure therapeutic usefulness, the weight variation test is a more straightforward substitute for the content uniformity test and serves as a gauge for differences in the drug's composition.

Table 3.9 shows the findings of the chemical content assay, which used UV spectrometry analysis to ascertain the quantity of ibuprofen contained in each brand. The range of the samples' Ibuprofen active component content was 94.637% to 98.450%. According to USP guidelines, the drug concentration in an assay should not exceed 110% and should not be less than 90%. Assay values of A-400 and F-400 brands of ibuprofen tablets were within the limits recommended by the USP. The two different brands of Ibuprofen tablets fulfilled the necessary requirement for active drug content, according to the laboratory findings. Thus, the drug's existence and compendial quality in products A and F were confirmed by the assay findings. The variations in the figures might be the result of various manufacturing processes and additives employed in various plants.

One of the most important factors in determining whether or not the tablets will be able to withstand breaking, chipping, or abrasion during handling, shipping, and storage is their hardness. Average hardness was found in the range of 3.28 ± 0.074% kg/ cm^2 (A brand) to 9.8± 0..234% kg/cm^2 (F brand). Tablet hardness of 4 kgF is considered to be the minimum for a satisfactory tablet. To provide resistance to damage during handling, packing, and transportation, tablets must have sufficient hardness. An excessively hard tablet would drastically reduce the breakdown period and, consequently, the dissolving rate, even though BP advises a crushing strength of 5–8 kg. Table 3.4 on tablet hardness demonstrated that every brand provided the maximum crushing strength advised by the BP. But a minimum hardness of 4 kg is required, and tablets with a high compact nature will be produced at a hardness of 6.0 kg or more. This has to do with the influence of one or more factors on hardness. Every brand of ibuprofen complies with USP specifications since its hardness is within an allowed range. Tablet density and porosity variations are reflected in variations in tablet hardness.

As one of the most important tablet properties, tablet hardness is typically evaluated as an in-process-control parameter during tablet manufacture. It characterizes the compatibility of tableting

materials and the mechanical strength of the tablet to withstand potential stresses during tableting packaging, shipping, and dispensing. Tablet hardness is not a perfect indicator of strength since certain tablets have a tendency to cap on attrition, losing their crown sections when squeezed into extremely hard tablets. Friability is another criterion of tablet strength that is frequently tested. According to the Pharmacopoeia (USP 30, NF 25), tablets should have a friability value of less than 1%. All ibuprofen brands here met this standard, which ranged from 0.146 to 0.215 % (**Table 3.5**). The brands studied did not have any tablets that cracked, split, or broke throughout the test, and their mean percentage weight loss was less than 1.0%. So, the brands showed compliance with BP 2005 specification. Based on the results of the Friability and Hardness tests as well as the quality evaluation, it can be concluded that the combination of additional drugs and excipients in the product formulations of the two firms results in significant differences.

The factor that determines how quickly a medicine is absorbed is the disintegration time. Drug breakdown and, in turn, its bioavailability might be impacted by the kind and quantity of excipients utilized by various manufacturers. Tablet crushing strength ratings could not be used to forecast the disintegration periods of the various brands. Ibuprofen tablets disintegration times ranged from 2.00 min (F brand) to 14.5 min (A brand), measured in minutes. (**Table 3.7**) The USP requirements were met by the two brands. The two brands' adequate disintegration times may be a sign of good bioavailability since the tablets will dissolve quickly in the gastrointestinal system, increasing the surface area available for medication absorption and dissolution. Because various manufacturers use different formulation procedures and excipients to modify the disintegration and release characteristics of their tablets, it is impossible to estimate the disintegration time based solely on the tablet hardness measurements. There is a tendency for tablets with higher hardness levels to dissolve faster. There is no correlation between hardness and disintegration time, according to this study. The drug particle size, variations in the excipients employed, and the formulation techniques used by various manufacturers can all give the tablet distinct properties whether it is in its solid or hydrated solution state. In reality, the link between tablet hardness and disintegration is complicated.

The solubility of the medication in the aqueous environment of the gastrointestinal system is a prerequisite for drug bioavailability, meaning that the medicine should not dissolve in its oral solid dose form. Assuring product homogeneity has led to the development of dissolving testing for solid oral medicinal formulations. The findings from the dissolution tests on the 50% time to dissolve and dissolving efficiency. A drug's pharmacological action is greatly influenced by its dissolving behavior. *In vitro-in vivo* correlation, so named because it is commonly accepted, refers to the established direct link between the in vitro dissolution rate of many medicines and their bioavailability. Depending on how they were made, solid dosage forms might or might not dissolve when they come into contact with gastrointestinal fluid after being taken orally. Two brands were found to satisfy the pharmacopoeia's dissolution test specifications based on the dissolution test findings. The findings showed that both brands have adequate drug release to the site of absorption and perhaps good bioavailability. Each product has unique dissolving qualities that differ between brands since there are several components that impact the dissolve when taken as a whole. Conversely, a brand's dissolution value indicated a significant variance in *in vitro* dissolution.

The physicochemical characteristics of the active components and excipients as well as the manufacturing process may have an impact on the product's formulation, which can have a major impact on the rate of disintegration and dissolution. The parameters of disintegration and dissolution are known to be influenced by the kind and quantity of excipients utilized in tablet formulation as well as the manufacturing method. Disintegration time, hardness, friability, weight variation, dissolving profile, and other quality criteria can all be significantly impacted by the way a pharmacological product is formulated. Together with the methods employed in the production process, this also covers the physiochemical characteristics of the excipients and active components. The disintegration and dissolution test findings (Table 3.7, 3.12) indicate that a large increase in disintegration enhanced the rate of drug release. Fu. *et al.* said that Orally Disintegrating Tablets (ODT) are made to dissolve and disintegrate quickly, and as a result, their porosity is usually high to facilitate quick water absorption. Despite having a very high hardness, the Ibuprofen tablet brands showed excellent quality evaluation characteristics, including dissolving profile, disintegration time, and chemical content determination. This suggests that the hardness test is not an important criterion for evaluating quality.

Consequently, it was determined that the studied ibuprofen tablet brands met compendial requirements in terms of weight uniformity, active component quantity, hardness, friability, disintegration time, and dissolving rate.

Chapter Five: Conclusion

Pharmaceutical items are becoming more and more necessary due to the expanding human population. The regulatory organizations are primarily concerned with the attributes. For the best possible safety and efficacy, pharmaceutical product quality requirements are crucial.

In terms of *in vitro* quality assessment tests of uniformity of hardness, thickness, diameter, weight, friability, disintegration time, and dissolving test, the two brands of traditional ibuprofen tablets were found to be in compliance with USP criteria, as far as the results of the current study are concerned. Quality assessments are required in order to avoid any contamination or mistakes. The specifications of the standards should also adhere to the quality specifications. With a few notable outliers, the examined samples satisfied the BP and USP requirements for quality.

Such quality assessment may also be particularly crucial in underdeveloped nations where the provision of healthcare services has been severely hampered by the prevalence of fake and inferior medications. A bioavailability or bioequivalence investigation is necessary to determine their true therapeutic efficacy.

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