STUDY OF PHARMACEUTICAL EQUIVALENCE OF DIFFERENT BRANDS OF NAPROXEN (500mg) TABLET

Submitted by:

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2007-3-70-018

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A thesis report submitted to the Department of Pharmacy, East West University, Bangladesh, in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy

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This Thesis Paper is dedicated to My Parents& my husband

The thesis paper on "Study of pharmaceutical equivalence of different brands of naproxen (5oomg) tablet" submitted to Department of Pharmacy, East West University, Dhaka in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy by Sabrina Afrin(2007-3-70-018)on December 2011.

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CERTIFICATE

This is to certify that the thesis "Study of pharmaceutical equivalence of different brands of naproxen (5oomg) tablet" submitted to the Department of Pharmacy, East West University, Mohakhali, Dhaka in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy (B.Pharm) was carried out by Sabrina Afrin (2007-3-70-018) under my guidance and supervision and that no part of the thesis has been submitted for any other degree. I further certify that all the sources of information and laboratory facilities availed of this connection is duly acknowledged.

.....

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Abstract

The quality of pharmaceutical finished dosage forms is of major concern to the pharmaceutical industries. An important aspect of the development of any pharmaceutical product is to maintain the quality standards of the product. Pharmaceutical preparations take many shapes and forms and are administered through variety of routes. Oral solid dosage forms particularly the tablet dosage form is the most well known of all. Tablet dosage form of any pharmaceutical company goes through many research studies and experiments to maintain the proper quality standards. Different quality control tests are done to ensure quality product. **Aim:** The aim of this study was to investigate the quality of different brands of naproxen tablets which are manufactured in Bangladesh. Different physical parameters like hardness, thickness, friability test were conducted to evaluate the quality of the tablets of different brands of naproxen. To assess its effectiveness potency test was conducted. **Method:** Four different brands of Naproxen 500 mg were collected from the local market of Bangladesh. These were evaluated through the Quality control test(Hardness, thickness, friability test& potency test).**Result & discussion:** The range of hardness test result was 5-8kg. The friability test results were all in range of the standard value. The thickness results are in range. The potency value of all brands of naproxen tablet showed the standard value except Sonap, which is very poor (56.1%). **Conclusion:** Quality of a product is the major issue for any pharmaceutical company. To ensure quality product a pharmaceutical industry follows the international standards. So it can be said that quality is the main theme of any product. So to maintain the proper quality, quality control parameters must be followed.

CHAPTER - 01

Introduction

1.1 NSAIDs (Non steroidal anti inflammatory drugs):

The NSAIDs are group of chemically dissimilar agents that differ in their antipyretic & anti-inflammatory activities. They act primarily by inhibiting the cyclooxygenase enzymes that catalyze the 1st step in prostanoid biosynthesis. This leads to decreased prostaglandin synthesis with both beneficial & unwanted effect. Long-term treatments with COX-2 specific inhibitors have been shown to increase the risks of myocardial infarction & strokes, & several of these drugs have been withdrawn. Many experts believe that long-term therapy with older, nonspecitic NSAIDs (not including aspirin) may also cause similar problems. Patients are now advised to take the lowest dose that is effective for as short a period as possible. (Harvey, R.A. & Champe, P.C.,2006)

1.2 Classification of NSAIDs drugs-

A. Nonselective COX inhibitors(conventional NSAIDs)

1. Salicylates: Aspirin, Diflunisal

2 .Pyrazolone derivatives: Phenylbutazone, Oxyphenylbutazone.

3. Indole derivatives: Indomethacin, Sulindac.

4. Propionic acid derivatives: Ibuprofen, Naproxen, ketoprofen.

5. Anthranilic acid derivatives: Mephenamic acid

6 .Aryl -acetic acid derivatives:Diclofenac

7. Oxicam derivatives:Piroxicam, Tenoxicam.

8. Pyrrolo-pyrrole derivative:Ketorolac.

B .Preferential COX-2 inhibitors: Nimeslide,Meloxicam, Nabumetone.

C. Selective COX-2 inhibitors: Celecoxib,Rofecoxib, valdecoxib

D. Analgesic-antipyretics with poor anti-inflammatory action

1. Paraaminophenol derivative: Paracetamol

2. Pyrazolone derivatives:Metamizol, Propiphenazone.

3. Benzoxazocine derivative: Nefopam.(Tripathi,K.D.,2008)

1.3 Naproxen

Naproxen is a proprionic acid derivative related to the arylacetic acid group of nonsteroidal anti-inflammatory drugs. Naproxen is commonly used for the reduction of mild to moderate pain, fever, inflammation and stiffness caused by conditions such as osteoarthritis, rheumatoid arthritis, psoriatic arthritis, gout, ankylosing spondylitis, injury, menstrual cramps, tendinitis, bursitis, and the treatment of primary dysmenorrhea.

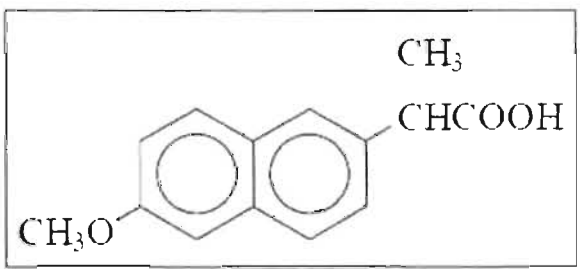
Naproxen works by blocking the cyclo-oxygenase which is involved in the production of certain irritant chemicals in response to injury or disease. By blocking the action of COX, naproxen reduce the symptoms of pain and inflammation. Some forms of naproxen have a special enteric coating to help protect stomach against irritation. There is also a modified-release form of tablets which allows naproxen to be released slowly to give a more even pain-relieving effect. Naproxen can be used alone, or alongside medicines such as misoprostol or esomeprazole which help protect against stomach irritation.

1.4 Chemistry of naproxen

Chemical name :(S)-6-methoxy-α-methyl-2-naphthaleneacetic acid;

Empirical formula: $C_{14}H_{14}O_3$.

Structural formula of naproxen:

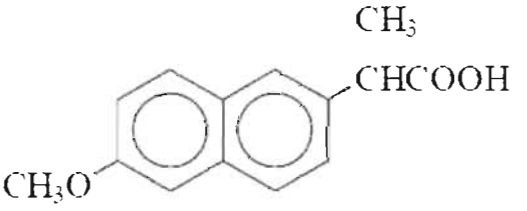


- Molecular weight: 230.2628.
- Solubility & pH: It is lipid-soluble, practically insoluble in water with a low pH (below pH 4), while freely soluble in water at 6 pH and above.
- Melting point: 153 °C.
- Odor: It is odorless
- Colour: white to off white, crystalline substance.(Mosby,2000)

1.5 History of naproxen:

Naproxen was first sold as the prescription drug Naprosyn in 1976; naproxen sodium was first sold under the trade name Anaprox in 1980. The Food and Drug Administration (FDA) approved naproxen sodium's use as an over-the-counter drug in 1994. Naproxen is still a prescription drug in much of the world

1.6 Structure activity relationship:



Structure of naproxen

In a series of substitution 2-naphthylacetic acids, substitution in the 6-position led to maximum anti-inflammatory activity. Small lipophilic groups such as Cl,CH_3S,&CHF_2O were active analogue with CH_3O being the most potent. Larger groups were found to be less active. Derivatives of 2-nahthylpropionic acids are more potent than the corresponding acetic acid analogues. Replacing the carboxyl group with functional groups capable of being metabolized to the carboxyl function (e.g, -CO_2CH_3,-CHO or –CH_2OH) led to a retention of activity.

The (S)(+)isomer is more potent enantiomer .Naproxen is the only arylalkanoic acid NSAID marketed as optically active isomers.(Willium D.A., 2007)

1.7 Mechanism of action

Naproxen inhibite the cyclooxygenase activity. There are two form of cyclooxygenase ,termed COX-1 & COX-2. COX-1 is expressed in all tissue & responsible for the production of protective prostaglangins in the kidney & stomach as well as the functional thromboxane of platelets. The constitutive cyclooxygenase, COX-1, synthesizes prostaglandins necessary for normal gastrointestinal and renal function. COX-2 not found in most tissues, expressed under condition of tissue damage & plays an active role in the inflammatory response. The inducible cyclooxygenase, COX-2, generates prostaglandins involved in inflammation. Inhibition of COX-1 is thought to be associated with gastrointestinal and renal toxicity while inhibition of COX-2 provides anti-inflammatory activity (Harvey, R.A. & Champe, P.C. 2006)

1.8 Therapeutic activity

Naproxen is usually indicated for the treatment of acute or chronic conditions where pain and inflammation are present. Research continues into their potential for prevention of colorectal cancer, and treatment of other conditions, such as cancer and cardiovascular disease.

Naproxen is generally indicated for the symptomatic relief of the following conditions:

- Rheumatoid arthritis
- Osteoarthritis
- Inflammatory arthropathies (e.g. ankylosing spondylitis, psoriatic arthritis, Reiter's syndrome)
- Acute gout
- Dysmenorrhoea (menstrual pain)
- Metastatic bone pain
- Headache and migraine
- Postoperative pain

- Mild-to-moderate pain due to inflammation and tissue injury
- Pyrexia (fever)
- Renal colic (Brunton, et al., 2006).

1.9 Pharmacokinetics

Naproxen is rapidly and completely absorbed from the gastrointestinal tract with an in vivo bioavailability of 95%. The elimination half-life of naproxen ranges from 12 to 17 hours. Steady-state levels of naproxen are reached in 4 to 5 days, and the degree of naproxen accumulation is consistent with this half-life.

1.9.1 Absorption

After administration of naproxen tablets, peak plasma levels are attained in 2 to 4 hours.

1.9.2 Distribution

Naproxen has a volume of distribution of 0.16 L/kg. At therapeutic levels naproxen is greater than 99% albumin-bound. At doses of naproxen greater than 500 mg/day there is less than proportional increase in plasma levels due to an increase in clearance caused by saturation of plasma protein binding at higher doses (average trough C_{ss} 36.5, 49.2 and 56.4 mg/L with 500, 1000 and 1500 mg daily doses of naproxen, respectively). The naproxen anion has been found in the milk of lactating women at a concentration equivalent to approximately 1% of maximum naproxen concentration in plasma

1.9.3 Metabolism

Naproxen is extensively metabolized in the liver to 6-0-desmethyl naproxen, and both parent and metabolites do not induce metabolizing enzymes. Both naproxen and 6-0-desmethyl naproxen are further metabolized to their respective acylglucuronide conjugated metabolites.

1.9.4Excretion

The clearance of naproxen is 0.13 mL/min/kg. Approximately 95% of the naproxen from any

dose is excreted in the urine, primarily as naproxen (< 1%), 6-0-desmethyl naproxen (< 1%) or their conjugates (66% to 92%). The plasma half-life of the naproxen anion in humans ranges from 12 to 17 hours. The corresponding half-lives of both naproxen's metabolites and conjugates are shorter than 12 hours, and their rates of excretion have been found to coincide closely with the rate of naproxen disappearance from the plasma. Small amounts, 3% or less of the administered dose, are excreted in the feces. In patients with renal failure metabolites may accumulate

1.10 Pharmacodynamics

Naproxen is a non-steroidal anti-inflammatory drug (NSAID) with analgesic and antipyretic properties. The sodium salt of naproxen has been developed as a more rapidly absorbed formulation of naproxen for use as an analgesic. The mechanism of action of the naproxen anion, like that of other NSAIDs, is not completely understood but may be related to prostaglandin synthetase inhibition

1.11 Naproxen side effects

Naproxen has some severe side effect. Like-

- chest pain, weakness, shortness of breath, slurred speech, problems with vision or balance;
- black, bloody, or tarry stools;
- coughing up blood or vomit that looks like coffee grounds;
- swelling or rapid weight gain;
- urinating less than usual or not at all;
- nausea, stomach pain, low fever, loss of appetite, dark urine, clay-colored stools, jaundice (yellowing of the skin or eyes);
- fever, sore throat, and headache with a severe blistering, peeling, and red skin rash;
- bruising, severe tingling, numbness, pain, muscle weakness; or
- fever, headache, neck stiffness, chills, increased sensitivity to light, purple spots on the skin, and/or seizure (convulsions).

Less serious naproxen side effects may include:

- upset stomach, mild heartburn or stomach pain, diarrhea, constipation;
- bloating, gas;
- dizziness, headache, nervousness;
- skin itching or rash;
- blurred vision; or
- ringing in your ears.

1.12 Adverse effect :.

✓ In patients taking naproxen in clinical trials, the most frequently reported adverse experiences in approximately 1% to 10% of patients are:

Gastrointestinal (GI) Experiences, including: heartburn Incidence of reported reaction between 3% and 9%. Those reactions occurring in less than 3% of the patients are unmarked. abdominal pain, nausea, constipation, diarrhea, dyspepsia, stomatitis

Central Nervous System: headache, dizziness, drowsiness, lightheadedness, vertigo

Dermatologic: pruritus (itching), skin eruptions, ecchymoses, sweating, purpura

Special Senses: tinnitus, visual disturbances, hearing disturbances

Cardiovascular: edema, palpitations

General: dyspnea, thirst

✓ In patients taking NSAIDs, the following adverse experiences have also been reported in approximately 1% to 10% of patients.

Gastrointestinal (GI) Experiences, including: flatulence, gross bleeding/perforation, GI ulcers (gastric/duodenal), vomiting

General: abnormal renal function, anemia, elevated liver enzymes, increased bleeding time, rashes

- ✓ The following are additional adverse experiences reported in <1% of patients taking naproxen during clinical trials and through postmarketing reports. Those adverse reactions observed through postmarketing reports are italicized.

Body as a Whole: anaphylactoid reactions, angioneurotic edema, menstrual disorders, pyrexia (chills and fever)

Cardiovascular: congestive heart failure, vasculitis, hypertension, pulmonary edema

Gastrointestinal: gastrointestinal bleeding and/or perforation, hematemesis, pancreatitis, vomiting, colitis, nonpeptic gastrointestinal ulceration, ulcerative stomatitis, esophagitis, peptic ulceration

Hepatobiliary: jaundice, abnormal liver function tests, hepatitis (some cases have been fatal)

Hemic and Lymphatic: eosinophilia, leucopenia, melena, thrombocytopenia, agranulocytosis, granulocytopenia, hemolytic anemia, aplastic anemia

Metabolic and Nutritional: hyperglycemia, hypoglycemia

Nervous System: inability to concentrate, depression, dream abnormalities, insomnia, malaise, myalgia, muscle weakness, aseptic meningitis, cognitive dysfunction, convulsions

Respiratory: eosinophilic pneumonitis, asthma

Dermatologic: alopecia, urticaria, skin rashes, toxic epidermal necrolysis, erythema multiforme, erythema nodosum, fixed drug eruption, lichen planus, postular reaction, systemic lupus erythematoses, Stevens-Johnson syndrome, photosensitive dermatitis, photosensitivity reactions, including rare cases resembling porphyria cutanea tarda (pseudoporphyria) or epidermolysis bullosa. If skin fragility, bulering or other symptoms suggestive of pseudoporphyria occur, treatment should be discontinued and the patient monitored.

Special Senses: hearing impairment, corneal opacity, papillitis, retrobulbar optic neuritis, papilledema

Urogenital: glomerular nephritis, hematuria, hyperkalemia, interstitial nephritis, nephrotic syndrome, renal disease, renal failure, renal papillary necrosis, raised serum creatinine

Reproduction (female): infertility

- ✓ In patients taking NSAIDs, the following adverse experiences have also been reported in < 1% of patients.

Body as a Whole: fever, infection, sepsis, anaphylactic reactions, appetite changes, death

Cardiovascular: hypertension, tachycardia, syncope, arrhythmia, hypotension, myocardial infarction

Gastrointestinal: dry mouth, esophagitis, gastric/peptic ulcers, gastritis, glossitis, eructation

Hepatobiliary: hepatitis, liver failure

Hemic and Lymphatic: rectal bleeding, lymphadenopathy, pancytopenia

Metabolic and Nutritional: weight changes

Nervous System: anxiety, asthenia, confusion, nervousness, paresthesia, somnolence, tremors, convulsions, coma, hallucinations

Respiratory: asthma, respiratory depression, pneumonia

Dermatologic: exfoliative dermatitis

Special Senses: blurred vision, conjunctivitis

Urogenital: cystitis, dysuria, oliguria/polyuria, proteinuria

1.13 Strengths of Naproxen

Prescription-strength naproxen is available in the following strengths.

- Naproxen 250 mg tablets

- Naproxen 375 mg tablets (immediate, delayed, and extended-release)
- Naproxen 500 mg tablets (immediate, delayed, and extended-release)
- Naproxen 125 mg/5 mL oral suspension -- one teaspoon (5 mL) contains 125 mg of naproxen Naproxen Sodium 275 mg tablets
- Naproxen Sodium 550 mg tablets.

1.14 Indication & usage

Naproxen is indicated for the treatment of rheumatoid arthritis, juvenile arthritis, ankylosing spondylitis, tendinitis & bursitis,& acute gout. It is also indicated in the relief of mild to moderate pain, & for the treatment of primary dysmenorrhea.

1.15 Contraindication:

Naproxen tablets are contraindicated in patients with known hypersensitivity to naproxen. It is also contraindication in patient in whom aspirin or other nonsteroidal anti-inflammatory/ analgesic drugs induce the syndrome of asthma,rhinitis,& nasal polyps. Both type of reaction have the potential of being fatal. Anaphylactoid reaction to naproxen whether of the true allergic type to pharmacologic idiosynertic (e.g, aspirin syndrome) type. Usually but not always occur in patients with a known history of such reaction. Therefore careful questioning of patient for such things as asthma, nasal polyps, urticaria, & hypotension associated with NSAIDs before starting therapy is important. In addition,if such symptoms occur during therapy ,treatment should be discontinued.(Mosby,2000)

1.16 Interaction:

The following sections explain in detail the potentially negative interactions that can occur if naproxen is combined with any of the substances listed above.

ACE Inhibitors

Combining naproxen with an ACE inhibitor can increase the risk of kidney problems (especially in people that already have kidney problems) and can decrease the effectiveness of the ACE inhibitor for lowering blood pressure.

ARBs

Combining naproxen with an ARB can increase the risk of kidney problems, especially in people who already have kidney problems, and can decrease the effectiveness of the ARB for lowering blood pressure.

Beta Blockers

Combining naproxen with a beta blocker may interfere with the beta blocker's ability to lower blood pressure. Check with your healthcare provider before taking these medications together.

Bile Acid Sequestrants

Bile acid sequestrants can bind to naproxen in the digestive tract and delay its absorption into the body. To avoid this drug interaction, naproxen should be taken at least one hour before or four to six hours after the bile acid sequestrant has been taken.

Corticosteroids

Using corticosteroids with naproxen can increase the risk of bleeding. Your healthcare provider may choose to monitor you more closely or adjust your dose of these drugs.

Cyclosporine

Naproxen may increase the level of cyclosporine in the blood, increasing the risk of serious side effects of cyclosporine. In addition, this combination may increase the risk of kidney damage. Check with your healthcare provider before taking these medications together.

Digoxin

Naproxen may increase the level of digoxin in your bloodstream, increasing the risk of dangerous side effects of digoxin. If you are taking digoxin, check with your healthcare provider before starting or stopping naproxen.

Diuretics

Combining naproxen with a diuretic can increase the risk of kidney problems, especially in people who already have kidney problems, and can decrease the effectiveness of the diuretic.

Lithium

Taking naproxen and lithium together may increase the levels of lithium in your body by reducing the kidneys' ability to remove lithium. Your healthcare provider may need to adjust your dose of these drugs and monitor the level of lithium in your blood.

"Blood Thinners" and Other Similar Drugs

Combining naproxen with anticoagulants ("blood thinners"), antiplatelet drugs, or other medications that increase the risk of bleeding may lead to serious bleeding problems, including dangerous internal bleeding. Do not combine naproxen with such medications without your healthcare provider's approval and supervision.

Methotrexate

Naproxen may increase the risk of methotrexate toxicity. Do not combine these medications without your healthcare provider's supervision and approval.

Probenecid

Combining probenecid and naproxen may increase the levels of naproxen in the blood. Therefore, your healthcare provider may recommend a lower naproxen dosage and monitor you more closely.

SSRIs or SNRIs

Combining a selective serotonin reuptake inhibitor (SSRI) or a serotonin-norepinephrine reuptake inhibitor (SNRI) with naproxen may increase the risk of bleeding. Check with your healthcare provider before taking naproxen with an SSRI or SNRI.

Herbal and/or Nutritional Supplements

Several herbal and nutritional supplements can also interact with naproxen and may increase the risk of bleeding. If you are taking any natural or herbal supplements, make sure to discuss this with your healthcare provider before starting naproxen therapy.

1.17 Pregnancy

1.17.1 Labour and Delivery

In rat studies with NSAIDs, as with other drugs known to inhibit prostaglandin synthesis, an increased incidence of dystocia, delayed parturition, and decreased pup survival occurred. Naproxen-containing products are not recommended in labor and delivery because, through its prostaglandin synthesis inhibitory effect, naproxen may adversely affect fetal circulation and inhibit uterine contractions, thus increasing the risk of uterine hemorrhage. The effects of naproxen on labour and delivery in pregnant women are unknown.

1.17.2 Nursing Mothers

The naproxen anion has been found in the milk of lactating women at a concentration equivalent to approximately 1% of maximum naproxen concentration in plasma. Because of the possible adverse effects of prostaglandin-inhibiting drugs on neonates, use in nursing mothers should be avoided.

1.17.3 Paediatric Use

Safety and effectiveness in paediatric patients below the age of 2 years have not been established. Pediatric dosing recommendations for juvenile arthritis are based on well-controlled studies. There are no adequate effectiveness or dose-response data for other pediatric conditions, but the experience in juvenile arthritis and other use experience have established that single doses of 2.5 to 5 mg/kg, with total daily dose not exceeding 15 mg/kg/day, are well tolerated in paediatric patients over 2 years of age.

1.17.4 Geriatric Use:

Studies indicate that although total plasma concentration of naproxen is unchanged, the unbound plasma fraction of naproxen is increased in the elderly. Caution is advised when high doses are required and some adjustment of dosage may be required in elderly patients. As with other drugs used in the elderly, it is prudent to use the lowest effective dose.

Experience indicates that geriatric patients may be particularly sensitive to certain adverse effects of nonsteroidal anti-inflammatory drugs. Elderly or debilitated patients seem to tolerate peptic ulceration or bleeding less well when these events do occur. Most spontaneous reports of fatal GI events are in the geriatric population

Naproxen is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function. Geriatric patients may be at a greater risk for the development of a form of renal toxicity precipitated by reduced prostaglandin formation during administration of nonsteroidal anti-inflammatory drugs

1.18 Overdose

Significant naproxen overdosage may be characterized by lethargy, dizziness, drowsiness, epigastric pain, abdominal discomfort, heartburn, indigestion, nausea, transient alterations in liver function, hypoprothrombinemia, renal dysfunction, metabolic acidosis, apnea, disorientation or vomiting. Gastrointestinal bleeding can occur. Hypertension, acute renal failure, respiratory depression, and coma may occur, but are rare. Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs, and may occur following an overdose. A few patients have experienced convulsions, but it is not clear whether or not these were drug-related. It is not known what dose of the drug would be life threatening. The oral LD_{50} of the drug is 543 mg/kg in rats, 1234 mg/kg in mice, 4110 mg/kg in hamsters, and greater than 1000 mg/kg in dogs.

Patients should be managed by symptomatic and supportive care following a NSAID overdose. There are no specific antidotes. Hemodialysis does not decrease the plasma concentration of naproxen because of the high degree of its protein binding. Emesis and/or activated charcoal (60

to 100 g in adults, 1 to 2 g/kg in children) and/or osmotic cathartic may be indicated in patients seen within 4 hours of ingestion with symptoms or following a large overdose. Forced diuresis,

alkalinization of urine or hemoperfusion may not be useful due to high protein binding.(Mosby,2000)

1.19 Quality

Quality is essential for the survival and growth of any organization. Quality signifies excellence of a product or service, which is measured, based on customer's experience with the product or service against his or her requirements. The quality of a product may be defined as "its ability to fulfill the customer's needs and expectations". Quality needs to be defined firstly in terms of parameters or characteristics, which vary from product to product. For example, for a mechanical or electronic product these are performance, reliability, safety and appearance. For pharmaceutical products, parameters such as physical and chemical characteristics, medicinal effect, toxicity, taste and shelf life may be important. For a food product they will include taste, nutritional properties, texture and shelf life etc (Waleed, et al., 2001).

1.20 Quality of pharmaceutical products

Quality of product is the main precursor for any pharmaceutical industry to maintain its existence. In pharmaceutical industry, the quality is a measure of high degree of managerial, scientific and technical sophistication. Quality is always an obligatory prerequisite when we consider any product. It becomes primary when it relates to life saving products like pharmaceuticals. Although it is mandatory from the government and regulatory bodies but it is also a fact that quality of a pharmaceutical product cannot be adequately controlled solely by pharmacopoeia analysis of the final product. Today quality has to be built in to the product right from its inception and rigorous international environmental, safety and regulatory standards need to be followed. Validation had proven to be an important tool for quality management of pharmaceuticals (Aulton, 2002).

Most traditional pharmaceutical drugs are relatively simple molecules that have been found primarily through trial and error to treat the symptoms of a disease or illness. Over period of time these molecules were perfected to ensure quality. The quality is very much related to every pharmaceutical product. Without quality pharmaceutical drug cannot be marketed or sold, because it can cause many problems such as sub therapeutic or over dose.

If a drug of any brand or company does not maintain it then may cause serious problems when prescribed to the patients. The patients may suffer from the adverse effects because of its faulty quality which may sometimes prove to be fatal.

1.21 Quality control

The term "quality control" comprises of two words quality and control. Control is a universal regulatory process. In the industry, it takes the form of meeting standards. The process through which we establish and meet standards is called "control". Quality control deals with a system which accepts or rejects any activities which affect the Quality and prevents Quality deficiency and imparts consistency in the quality of the product or service (Marayya, 2005).

Quality is important in every product or service but it is vital in medicine as it involves life. Quality control is a concept which strives to produce a perfect product by a series of measures designed to prevent and eliminate errors at different stages of production. Although the responsibility for assuring product quality belongs principally to quality assurance personnel, it involves many departments and disciplines within a company. The quality of products is dependent upon that of the participating constituents, some of which are sustainable and effectively controlled while others are not.

To be effective, it must be supported by a team effort. Quality must be built into a drug product during product and process design, and it is influenced by the physical plant design, space, ventilation, cleanliness, and sanitation during routine production. The product and process design begins in research and development. It also includes preformulation and physical, chemical, therapeutic and toxicologic considerations (Lachman, 2008).

1.22 Quality assurance:

Design, development and implementation of quality assurance is the most vital function in the pharmaceutical industry. In pharmaceutical industry, the quality is a measure of a high degree of managerial, scientific and technical sophistication. Quality assurance is a wide-ranging concept

covering all matters that individually or collectively influence the quality of a product. It is the totality of arrangements made with the object of ensuring that pharmaceutical products are of the quality required for their intended use (Marayya and Anjaneyulu, 2005).

Quality control emphasizes testing of products to uncover defects, and reporting to management who make the decision to allow or deny the release, whereas quality assurance attempts to improve and stabilize production, and associated processes, to avoid, or at least minimize, issues that led to the defects in the first place. The assurance of product quality depends on more than just proper sampling and adequate testing of various components and the finished dosage form. Prime responsibility of maintaining product quality during production rests with the manufacturing department. Removal of responsibility from manufacturing for producing a quality product can result in imperfect composition, such as ingredients missing, subpotent or superpotent addition of ingredients, or mixing of ingredients; mistakes in packaging or filling, such as product contamination, mislabeling, or deficient package; and lack of conformance to product registration. Quality assurance personnel must establish control or checkpoints to monitor the quality of the product as it is processed and upon completion of manufacture.

Because of the increasing complexity of modern pharmaceutical manufacturing arising from a variety of unique drugs and dosage forms, complex ethical, logical and economic responsibilities have been placed on those concerned with the manufacture of modern pharmaceuticals. An awareness of these factors is the responsibility of all those involved in the development, manufacture, control, and marketing of quality products (Lachman, 2009).

1.23 Quality control parameters:

Solid dosage forms are most important when drug administration is concerned. Among the solid dosage forms tablet is main attraction for the patients. Tablet is the most advantageous over all the other solid dosage forms. So tablets have to be a proper quality product. To maintain the quality of tablet dosage form, quality control parameters are truly needed. For tablets, there are several quality control parameters which are used in the pharmaceutical industry to make effective and quality tablets. The quality control parameters are known as hardness test, thickness test, friability test, weight variation test, disintegration test etc. Some other tests are

also done to check the release profile of the manufactured tablets such as dissolution test and potency determination test

1.24 Aim and objectives of the study

The aim and objectives of the study were-

- To analyze different brands of naproxen in terms of physical parameters like hardness test, thickness test, friability test, disintegration test etc.
- To determine the potency of selected brands of naproxen.
- To assess and compare the rates of dissolution among different brands of naproxen

Literature Review

1. Naproxen is licensed to reduce pain and inflammation caused by various conditions, such as injury, arthritis, and menstrual cramps. It works by inhibiting the action of certain hormones that cause inflammation and pain in the body. Naproxen is available as either an over-the-counter or prescription drug, and comes in tablet, caplet, or liquid form. Human clinical trials have shown the clinical activity of 500 mg of naproxen daily to be similar to that of 3.6 g of ASA daily. From clinical trials, it appears that naproxen enteric-coated tablets have reduced potential for severe complaints when compared to standard naproxen.

Kim YS et al conducted a study on 'Solubility and prediction of the heat of solution of sodium naproxen in aqueous solutions'. The solubility of sodium naproxen was determined over a range of temperatures from 15.2 degrees C to 39.7 degrees C by two methods: analyses of samples from equilibrated solutions and a recently developed procedure utilizing a focused-beam reflectance method (FBRM). The results demonstrate the utility of the newer and, in some cases, simpler method. A discontinuity in the solubility was observed at 29.8 degrees C, identifying the temperature as which the dihydrate and anhydrous forms of sodium naproxen trade places as being the more stable of the two forms. The heats of solution for the two pseudopolymorphs were obtained from van't Hoff plots of the solubility data. These results were used to demonstrate how the heat of solution of one form can be estimated using the heat of dehydration obtained from differential scanning calorimetry (DSC) and the heat of solution from another form. (Kim YS, Méndez del Río JR & Rousseau RW, 2005)

2. On the study of 'Naproxen release from sustained release matrix system and effect of cellulose derivatives', Sarfraz MK was conducted to investigate the low viscosity grades of hydroxypropylmethyl cellulose (HPMC) and ethyl cellulose (EC) in sustaining the release of water insoluble drug, naproxen from the matrix tablets. Both HPMC and EC were incorporated in the matrix system separately or in combinations by wet granulation technique. In vitro dissolution studies indicated that EC significantly reduced the rate of drug release compared to HPMC in 12 hour testing time. But, no significant difference was observed in the release profiles of matrix tablets made by higher percentages of EC. The tablets prepared with various combinations of HPMC and EC also failed to produce produce the desired release profiles.

However, comparatively linear and desirable sustained release was obtained from EC-based matrix tablets prepared by slightly modifying the granulation method. Moreover, two different compression forces used in tableting had no remarkable effect on the release profile of naproxen. (Sarfraz MK, Rehman NU & Mohsin S., 2006)

3. In 'Partial-solubility Parameters of Naproxen and Sodium Diclofenac' the expanded Hansen method was tested for determination of the solubility parameters of two non-steroidal anti-inflammatory drugs, naproxen and sodium diclofenac. This work describes for the first time the application of the method to the sodium salt of a drug. The solubility of both drugs was measured in pure solvents of several chemical classes and the activity coefficient was obtained from the molar heat and the temperature of fusion. Differential scanning calorimetry was performed on the original powder and on the solid phase after equilibration with the pure solvents, enabling detection of possible changes of the thermal properties of the solid phase that might change the value of the activity coefficient. The molar heat and temperature of fusion of sodium diclofenac could not be determined because this drug decomposed near the fusion temperature. The best results for both drugs were obtained with the dependent variable $\ln X_2$ in association with the four-parameter model which includes the acidic and basic partial-solubility parameters δ_a and δ_b instead of the Hansen hydrogen bonding parameter δ_h. Because the dispersion parameter does not vary greatly from one drug to another, the variation of solubility among solvents is largely a result of the dipolar and hydrogen-bonding parameters, a fact that is being consistently found for other drugs of small molecular weight. These results support earlier findings with citric acid and paracetamol that the expanded Hansen approach is suitable for determining partial-solubility parameters. The modification introduced in the expanded Hansen method, i.e. the use of $\ln X_2$ as the dependent variable, provides better results than the activity coefficient used in the original method. This is advantageous for drugs such as sodium diclofenac for which the ideal solubility cannot be estimated. This paper shows for the first time that the method is suitable for determination of the partial-solubility parameters of a sodium salt of a drug, sodium diclofenac (Bustamante P, Pena MA & Barra, J, 1998).

4. Maghsoodi M worked on 'Physicomechanical Properties of Naproxen-Loaded Microparticles Prepared from Eudragit L100'. Microparticles of naproxen with Eudragit L100 and Aerosil were prepared by the emulsion solvent diffusion method in order to avoid local gastrointestinal irritation, one of the major side effects of nonsteroidal anti-inflammatory drugs after oral ingestion. The process of preparation involved the use of ethanol as good solvent, dichloromethane as a bridging liquid, water as poor solvent, Aerosil as anti-adhesion agent, and sodium dodecyl sulfate to aid in the dispersion of the drug and excipients into the poor solvent. The obtained microparticles were evaluated for micromeritic properties, yield, encapsulation efficiency, drug physical state, and drug release properties. The influence of formulation factors and preparation condition (polymer/naproxen ratio, Aerosil/polymer ratio, and the initial difference of temperature between the solvent and nonsolvent) on the properties of the microparticles was also examined. The resultant microparticles were finely spherical and uniform with high incorporation efficiency (>79%) and yield (>71%). The incorporation efficiency was enhanced with increasing the ratio of excipients to drug and the initial difference of temperature between the solvent and nonsolvent. The mean diameter of the microparticles was influenced by all of the manufacturing parameters. Studies carried out to characterize the micromeritic properties of formulations, such as flowability and packability, showed that microparticles were suitable for further pharmaceutical manipulation (e.g., capsule filling). Drug release studies of the microparticles confirmed the gastroresistance, and mathematical studies showed that the drug released followed a Hixon and Crowell kinetic. These microparticles represent a simple method for the preparation of drug-loaded enteric microparticles with desired micromeritic properties and gastroresistance release. In the study of 'Particle design of naproxen-disintegrant agglomerates for direct compression by a crystallo-*co*-agglomeration technique', Maghsoodi M obtained directly compactible agglomerates of naproxen containing disintegrant by a novel crystallo-*co*-agglomeration (CCA) technique. Acetone–water containing hydroxypropylcellulose (HPC) was used as the crystallization medium. Acetone acted as a good solvent for naproxen as well as a bridging liquid for agglomeration of crystallized drug with disintegrant and aqueous phase as non-solvent. The agglomerates were characterized by differential scanning calorimetry (DSC), powder X-ray diffraction (XRPD) and scanning electron microscopy. The agglomerates were compressed at different compression pressures and

dissolution studies were carried out for the tablets produced at lowest compression force. The growth of particle size and the spherical form of the agglomerates resulted in formation of products with good flow and packing properties. The improved compaction properties of the agglomerated crystals were due to the fragmentation which occurred during compression. DSC and XRPD studies showed that naproxen particles, crystallized in the presence of HPC and disintegrant did not undergo structural modifications. The dissolution rate of naproxen from the agglomerates could be controlled by the amount of included disintegrant, being enhanced as the latter was increased. Moreover, the results showed that when the disintegrants were included both intragranularly and extragranularly during agglomeration of naproxen particles, tablets containing these agglomerates dissolved at a faster rate than the tablets containing crystallized naproxen with the same amount of disintegrant incorporated only extragranularly by physical mixing. In conclusion, the properties of agglomerated crystals, such as flowability, compactibility and dissolution rate were improved profoundly using the developed technique resulting in successful direct tableting without need to additional process of physical blending of agglomerates and disintegrants (Maghsoodi M, Taghizadeh O, Martin GP & Nokhodchi A., 2008).

5. The aim of 'Preparation & Physicochemical Characterization of Naproxen Tablets by Direct Compression Method' was to improve the flowability and compressibility of poorly compressible drug (Naproxen) which could be helpful for preparation of tablets by direct compression method; to characterize the molecular status of the drug in the tablet; to evaluate the mechanical properties of the compact; to evaluate the dissolution rate of the compact; conversion in solid (tablet) dosage form. Prototype formulation development was done by physically mixing Naproxen, MCC (PH101) and talcum in different ratios (1:1; 2:1; 3:1). Preparation of tablet by direct compression method was done using MCC (PH101) and talcum in different ratios and characterization of mechanical properties were done. Physicochemical characterization of the drug in the formulation was done by in vitro dissolution study; molecular interaction study. These studies resulted in enhanced flow ability, pack ability, compressibility, compactibility along with drug dissolution properties. The compaction process enhanced drug dissolution

relative to drug alone and also relative to corresponding loosely mixed physical mixtures (Patra, S. R., Giri, C. K. & Mallick, S., 2011).

6. Malaj L et al conducted a study on 'Compression behavior of anhydrous and hydrate forms of sodium naproxen.' The aim of the work was to investigate the technological properties and the compression behaviour of the anhydrous and hydrate solid forms of sodium naproxen. Among the hydrates, the following forms were studied: the monohydrate (MSN), obtained by dehydrating a dihydrated form (DSN) in each turn obtained by exposing the anhydrous form at 55% RH; a dihydrated form (CSN) obtained by crystallizing sodium naproxen from water, the tetrahydrated form (TSN) obtained by exposing the anhydrous form at 75% RH. The physico-chemical (crystalline form and water content), the micromeritic (crystal morphology and particle size) and the mechanical properties (Carr's index, apparent particle density, compression behaviour, elastic recovery and strength of compact) were evaluated. We made every effort to reduce differences in crystal habit, particle size and distribution, and amount of absorbed water among the samples, so that the only factors affecting their technological behaviour would be the degree of hydration and the crystalline structure. This study demonstrates a correlation between the compression behaviour and the water molecules present in the crystalline structures. The sites where water molecules are accommodated in the crystalline structure behave like weak points where the crystalline lattice yields under compression. The crystal deformability is proportional to the number of water molecules in these sites; the higher the water content, the higher the deformability, because the densification behaviour changes from a predominantly elastic deformation to a plastic behaviour. The deformability is responsible for a higher densification tendency that favours larger interparticle bonding areas that may explain the better tabletability of TSN and CSN (Malaj L, Censi R, Gashi Z & Di Martino P., 2010).

7. 'Solid-state characterization and dissolution properties of naproxen-arginine-hydroxypropyl-beta-cyclodextrin ternary system' was conducted by Mura P et al. Here, the effect of ternary complexation of naproxen, a poorly water soluble anti-inflammatory drug, with hydroxypropyl-beta-cyclodextrin and the basic aminoacid L-arginine on the drug dissolution properties has been investigated. Equimolar binary (drug-cyclodextrin or drug-arginine) and ternary (drug-

cyclodextrin-arginine) systems were prepared by blending, cogrinding, coevaporation, and characterized by differential scanning calorimetry, thermogravimetric analysis, FT-IR spectroscopy, X-ray diffractometry. The dissolution behavior of naproxen from the different products was evaluated by means of a continuous flow through method. The results of solid state studies indicated the presence of strong interactions between the components in ternary coevaporated and coground systems, which were both of totally amorphous nature. In contrast, the presence of either free drug or free arginine was detected when the third component (cyclodextrin or aminoacid) was physically mixed, respectively, to the drug-arginine binary system (as physical mixture, coevaporate, or coground product) or to the drug-cyclodextrin binary system (as physical mixture, coevaporate, or coground product). All ternary combinations were significantly ($P<0.001$) more effective than the corresponding binary drug-cyclodextrin and drug-arginine systems in improving the naproxen dissolution rate. The best performance in this respect was given by the ternary coevaporate, with about 15 times increase in terms of both drug relative dissolution rate and dissolution efficiency. The synergistic effect of the simultaneous use of arginine and cyclodextrin on the dissolution rate of naproxen was attributed to the combined effects of inclusion in cyclodextrin and salt formation, as well as to a specific role played by arginine in this interaction (Mura P, Bettinetti GP, Cirri M, Maestrelli F, Sorrenti M & Catenacci L, 2005).

CHAPTER - 2

Materials and Methods

2.1 Sample

From the entire Bangladeshi companies produce naproxen tablet, 4 brands were selected from 4 individual companies randomly. The name and brand of the selected companies are given below:

Table 2.1: Name and company of the selected brand of naproxen

Company	Brand
Sk +F	Naprox
Square	Sonap
Acme	Napro – A
Navana	Naxo
Delta pharma	Standard sample

2.2Hardness test

Tablet hardness is usually expressed as the load required crushing a tablet placed on its edge. Hardness is thus sometimes termed the tablet crushing strength. The suitability of a tablet in regard to mechanical stability during packaging and shipment can usually be predicted on the basis of hardness. Tablet hardness, in turn, influences tablet density and porosity. It may affect tablet friability and disintegration time. It usually affects drug dissolution and release and it may affect bioavailability.

Table 2.2: Name and specification of materials required in hardness test

Materials	Specification
Hardness tester	Monsanto Type hardness tester

Method:

1. The sliding scale of hardness tester has been set off to zero

2. The tablets have been placed vertically between the two jaws.

3. Force has been applied with the screw thread and spring until the tablets has been fractured.

4. A force of about 4-5 kg is considered to be the minimum for hardness according to The British Pharmacopoeia (Lachman, et al., 2008).

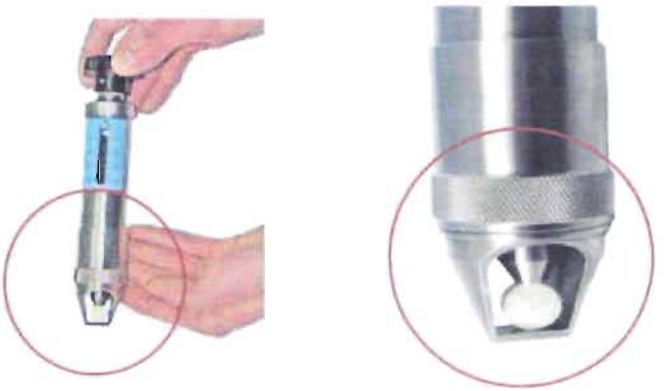


Figure 2.1: Monsanto Hardness tester

2.2 Friability test

Friction and shock are the forces that most often cause tablets to chip, cap or break. The friability test is closely related to tablet hardness and is designed to evaluate the ability of the tablet to withstand abrasion in packaging, handling and shipping. The value is expressed as a percentage. A maximum weight loss of not more than 1% of the weight of the tablets being tested during the friability test is considered generally acceptable and any broken or smashed tablets are not picked up. Normally, when capping occurs, friability values are not calculated. A thick tablet may have less tendency to cap whereas thin tablets of large diameter often show extensive capping, thus indicating that tablets with greater thickness have reduced internal stress.

Table 2.3: Name and specification of materials required to friability test.

Materials	Specification
Friability Tester	Friability Tester
Electronic Balance	Shimadzu, Japan

Method:

1. The experiment has been started by weighing 10 tablets which is considered as the initial reading

2. All the tablets have been placed in the drum of friability tester and rotate 100 times

3. The percentage loss has been calculated.

4. According to BP the tablets should not lose more than 1% of their total weight. (B.P. appendix: XVII, 2003)

Figure 2.2: Friability tester.

2.3Thickness test:

At constant compressive load, tablet thickness varies with change in die fill and tablet weight; with constant die fill, thickness varies with variations in compressive load. Some variation in tablet thickness in a particular lot of tablets or between different lots of the product is inevitable. Variation in tablet thickness should not be immediately apparent to the unaided eye under normal conditions, for obvious reasons of product acceptance by the consumer.

In general, tablet thickness is controlled within 5 percent of standard value. Tablet thickness control may be impossible unless (1) the physical properties of raw materials are closely controlled, (2) the upper and lower punch lengths are accurately and continuously standardized, (3) the granulation properties, including density, particle size, and particle size distribution are also carefully controlled .

Table 2.4: Name and specification of materials required to thickness test:

Materials	Specification
Vernier calliper	Shimadzu, Japan.

Method:

1. Tablets have been placed between two jaws horizontally.
2. The screw of the slide calipers has been ran to hold the tablets.

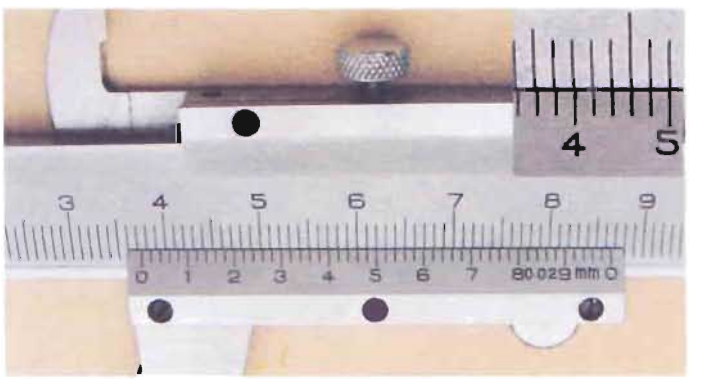


Figure 2.3: Vernier Callipers

2.5 Potency determination:

Potency is the strength of a dosage form. Potency determination is the chemical characteristics of a dosage form. The potency of official tablet is usually given in terms of milligrams of drug per tablet and is determined by means of an official analytical method which involves grinding several tablets in a mortar and analyzing a portion of the resulting powder (Lachman, et al., 2008).

Table 2.5: Name and source of materials required to determine sample potency

Materials	Specification
UV-Vis spectrophotometry	Hatch, USA.
Electronic Balance	ELB 3000, shimadzu. Japan.

Preparation of the standard solution:

50 mg of standard naproxen was weighed accurately in a 100 ml volumetric flask. 70 ml of methanol was added in it. It was shaked for 30 minutes and sufficient methanol was added to make volume up to 100ml. It was then mixed well and 10 ml of the solution was taken in a 50 ml volumetric flask. The volume was made up to 50 ml with methanol and mixed. 10 ml of the resulting solution was taken in a 100 ml volumetric flask and was added to volume up to the mark with methanol and mixed.

Method:

1. 2 tablets were weighed and crushed to make fine powder.
2. Take a quantity of the powder containing 50 mg naproxen in a 100 ml volumetric flask.
3. Add 70 ml methanol in the flask and shaked for 30 minutes and sufficient methanol was added to make volume up to 100 ml.
4. It was mixed well and then filtered.

5. 10 ml of the filtrate was taken in a 50 ml volumetric flask. The volume was made up to 50 ml with methanol and mixed.
6. 10 ml of the resulting solution was taken in a 100 ml volumetric flask and was added to volume up to the mark with methanol and mixed. (BP, 2003)

Measurement:

The absorbance of both the standard and assay solutions was measured in a suitable spectrophotometer having 1-cm quartz cell at 331 nm using methanol as blank.

The UV region consists of wavelengths from 200 to 400 nanometers (nm). The visible region extends from 400 to 800 nm, and the near IR (NIR) region covers 0.8 to 2.50 micrometers. Nanometer units are commonly used in the UV/VIS region, while micrometers or microns are normally used in the NIR region.

The Main Components of UV Analyzer:

Photometers and spectrophotometers can be used for on-line monitoring of process streams. These essential components are:

1. Source-provides radiation for the spectral region being measured.
2. Monochromator-a device used to select narrow bands of wavelengths.
3. Sample cell-contains the sample at an appropriate path length.
4. Detector-a device that measures transmitted energy and converts it into electrical energy.
5. Readout device-provides a means of recording the measurement results.

Figure 2.5: UV spectrophotometer.

Content Determination of the Samples

Content of naproxen can be measured by using the following equation,

Potency of naproxen =

$$\frac{\text{Wt. of STD} \times \text{abs. of sample} \times \text{dilution of sample} \times \text{potency of STD} \times \text{avg. wt. of tablet}}{\text{Wt. of sample} \times \text{abs. of STD} \times \text{dilution of STD}}$$

CHAPTER – 3

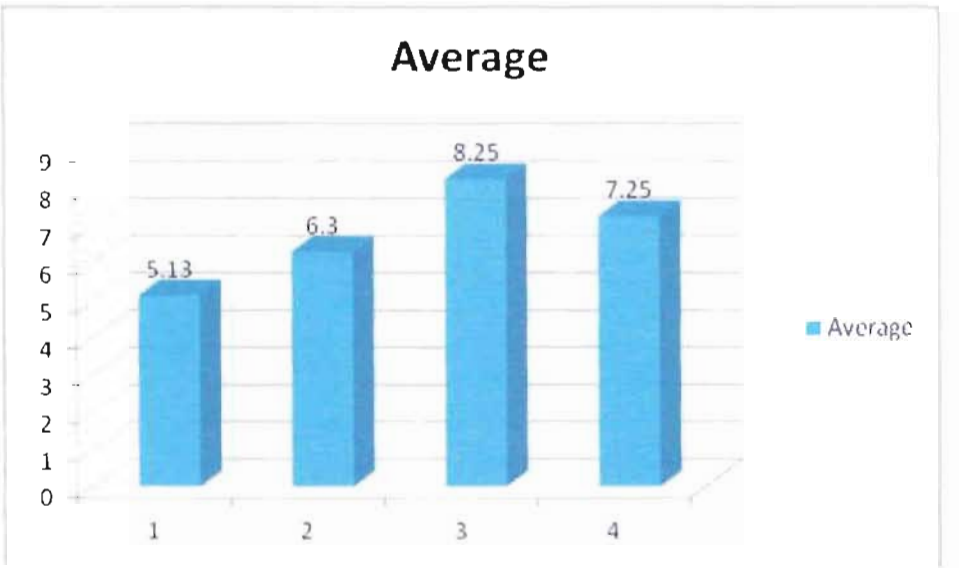
Results

3.1 Hardness Test:

Three tablets from each brand of naproxen were selected to conduct the hardness test. Test results were given below:

Table 3.1: result of hardness test

Brand name	Number of tablet	Hardness test(kg/cm)	Average
Napro A	1. 2. 3. 4. 5. 6.	5.5 5 4.9 5 5 5.4	5.13
Naprox 5oo	1. 2. 3. 4. 5. 6.	6.5 6.5 6.25 6.25 6.25 6	6.30
Naxo 500	1. 2. 3. 4. 5. 6.	8 8 8 8.5 9 8	8.25
Sonap	1. 2. 3. 4. 5. 6.	7.0 7.0 7.5 7.5 7.5 7.0	7.25



The highest value of hardness was Naxo500 (8.25). The lowest value of hardness was Napro A (5.13)

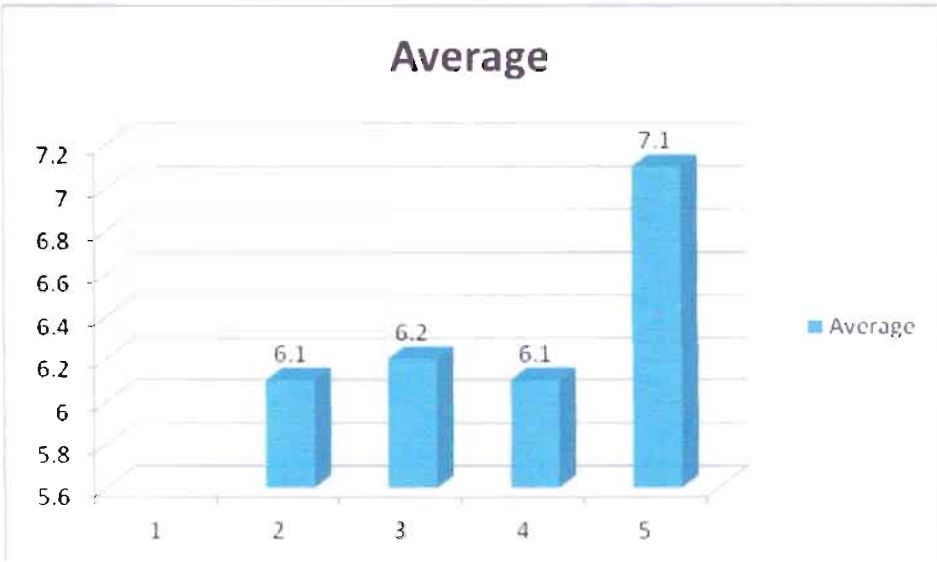
3.2 Thickness Test:

Tablets from each brand of naproxen were selected to conduct the thickness test. Test results were given below:

Table 3.2: result of thickness test

Brand name	Reading of scale (mm)	Reading of vernier scale(mm)	Vernier constant	Error	Thickness of the tablet	Average
Naprox 500	6 6 6 6 6 6	1 1 1 1 1 1	0.1 0.1 0.1 0.1 0.1 0.1	0	6.1 6.1 6.1 6.1 6.1 6.1	6.1
Naxo 500	6 6 6 6 6 6	2 2 2 2 2 2	0.1 0.1 0.1 0.1 0.1 0.1	0	6.2 6.2 6.2 6.2 6.2 6.2	6.2

Napro A	6 6 6 6 6 6	2.5 0 1.5 0.5 0.5 1.5	0.1 0.1 0.1 0.1 0.1 0.1	0	6.25 6 6.15 6.05 6.05 6.15	6.1
Sonap	7 7 7 7 7 7	1 1 1 1 1 1	0.1 0.1 0.1 0.1 0.1 0.1	0	7.1 7.1 7.1 7.1 7.1 7.1	7.1



The thickness of all the brands of naproxen was complied with the BP tandards. The highest value was Sonap(7.1) and the lowest value was Naprox 500(6.1) and Napro A (6.1).

3.3 Friability Test:

Ten tablets from each brand of naproxen were selected to conduct the friability test. Test results were given below:

Table 3.3: result of friability test

Brand	Initial weight of 10 tablets	Final weight of 10 tablets	Friability test (%)
Naprox 500	7.0415	7.0404	0.0156
Naxo 500	7.0692	7.0681	0.0155
Napro A	6.9514	6.9495	0.0273
Sonap	10.029	10.026	0.0299

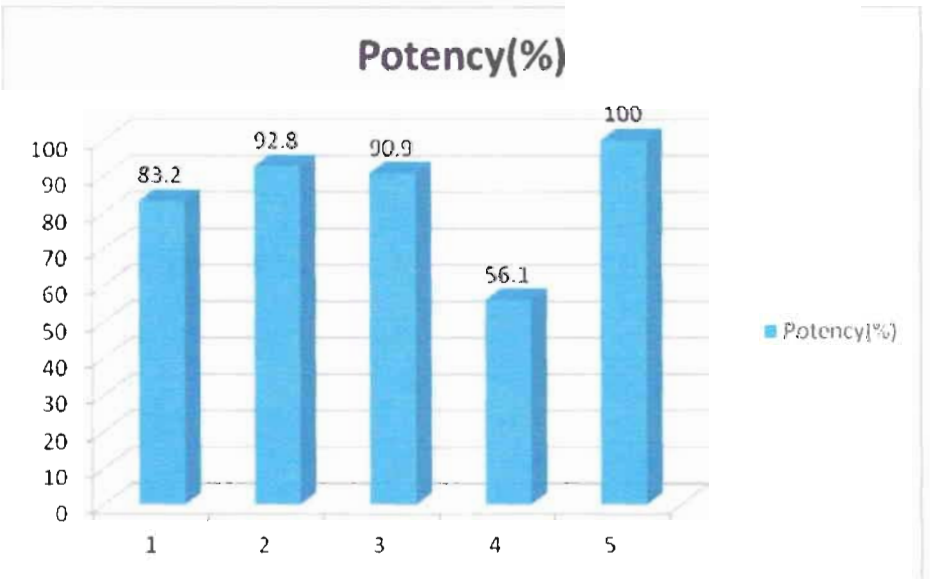
All the brands of naproxen has a in standard range friability values. The highest value was Sonap (o.o299%) & lowest value was Naxo 500 (0.0155%)

3.4 Potency test:

Two tablets from each brand of naproxen were selected to conduct the potency test. Test results were given below:

Table 3.4: result of the potency test

Tablet brand	Average weight of tablet (gm)	Absorbance of the sample	Weight of the sample (gm)	Potency(%)
Naprox 500	0.552	0.721	0.0552	83.2
Naxo 500	0.477	0.695	0.0477	92.8
Napro A	0.695	0.992	0.0695	90.9
Sonap	0.995	0.875	0.0995	56.1
Standard sample	o.500	0.785	0.0500	100



The potency determination test showed some higher and lower values. Compare with the standard sample (100%), the highest value is 92.8% (Naxo500) &the lowest value is 56.1% (Sonap).

CHAPTER - 04

Discussion and Conclusion

4.1 Discussion:

Quality Control is an essential function of the Pharmaceutical industry. Drug manufacturers must thoroughly test materials, processes, equipment, techniques, environments and personnel in order to ensure their final products are consistent, safe, effective and predictable. If a tablet is not a quality product than the dose as well as the manufacturing of the tablet can hamper. Also the tablet will have other problems such as hardness, thickness or disintegration.

Tablet Hardness testing is also called tablet breaking force and measures the tablet mechanical integrity. Hardness tests helps to measure whether a tablet inherits adequate hardness to withstand consumer handling and also provide satisfactory disintegration and dissolution results. Ideally all the different varieties of testing machines would give the same result if tablets of the same batch were used. In case of tablets from naproxen, the highest value of hardness was showed by Naxo 500(8.25).The lowest hardness value was showed by the brand Napro A(5.13) .High hardness causes the tablets to break slowly in the system, which is a major obstacle for the tablets to work efficiently.

Tablet thickness is an important quality control test for tablet packaging.Very thick tablet affects packaging either in blister or plastic container. Tablet thickness test provides an idea about the compressive strength during compression process. The highest and lowest value of thickness was 6.1(Naprox 500 & Napro A)and 7.1(Sonap) respectively. Difference between the thicknesses of the brands was quite small. Thickness was always an issue when tablets are considered. If the tablet is thicker than it cannot be swallowed by an average person. On the other hand, if the tablet is less thick then it can breakdown easily. So that thickness is important QC test.

Friction and shock are the forces that most often cause tablets to chip, cap or break. The friability test is closely related to tablet hardness and is designed to evaluate the ability of the tablet to withstand abrasion in packaging, handling and shipping. Conventional compressed tablets that lose less than 0.5 to 1 % of their weight are considered acceptable. From the graph, we can view that the % friability values for all the brands were within acceptable range. Difference between the brands friability percentage was quite small ,the highest friability value was 0.0299 % (Sonap) & lowest was 0.0155 %(Naxo 500).

Potency test is done for determine the quantity of active ingredient in the drug. In case of tablets of the different brands of naproxen, the highest value of potency was the brand Naxo 500(92.8%) and the lowest value of potency was the brand sonap (56.1%), which is very poor. The potency test differs due to the Analytical error, manufacturing error, tablet to tablet variation.

If a tablet contains more than its effective dose than it can cause overdose related complications. If a tablet contains less than its effective dose than it does not give desire effect. Right quantity of active ingredient in drug is necessary to give the desire effect of drugs.

4.2 Conclusion:

For the growing human population, pharmaceutical products necessities are increased rapidly. The qualities of these products are the prime concern for the regulatory bodies. Quality parameters of the pharmaceutical products are very important for optimum efficacy and safety. To prevent any contamination or errors quality control studies must be needed. The quality parameters also should be followed by the specification of the standards. Most of the tested samples met the quality specifications of BP standards with some exceptions. More extensive studies should be conducted to draw any conclusion regarding the quality of these brands considering the batch to batch variation. To understand their actual therapeutic effectiveness, bioavailability or bioequivalence study is essential.

CHAPTER- 05

References

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