Comparative Quality Control Test for Two Brand of Diclofenac Sodium &Paracetamol Tablet

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Abstract- Quality control is a critical aspect of the pharmaceutical industry, ensuring the identity, purity, safety, and efficacy of drug products. In this study, two types of combined diclofenac sodium and paracetamol tablets from different pharmaceutical companies were subjected to various quality control tests to determine their compliance with the standards specified in the Indian Pharmacopoeia. The evaluated parameters included weight variation, content uniformity, thickness, hardness, friability, disintegration time, dissolution rate, and pharmacopeial assay. The results indicated that all brands successfully met most of the pharmacopeial specifications. Both brands complied with the acceptable limits for weight variation and friability tests. However, variations were observed in hardness, disintegration time, and dissolution profiles among the tested samples. These differences may influence the therapeutic performance of the formulations. The study emphasizes that an ideal tablet should possess adequate hardness to maintain its mechanical integrity while ensuring optimal disintegration and dissolution for effective drug release and therapeutic action.

I.INTRODUCTION

Quality control

The concept of total energy quality control refers to the produce a perfect product by a series of measures requiring an organized effort by the entire company to prevent or eliminate errors at every stage in production. Although the responsibility for assuring product quality belongs principally to quality assurance personnel, it involves many departments and disciplined lines within a company. 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, and includes preformulation and physical, chemical, therapeutic, and toxicological considerations. It considers materials, in process and product control, including specifications and tests for the active ingredients, the excipients, and the product itself, specific stability procedures for the product, freedom from microbial contamination and proper storage of the product, and containers, packaging and labeling to ensure that container closure systems provide functional protection of the product against such factors as moisture, oxygen, light, volatility, and drug/package interaction. Provision for a cross referencing system to allow any batch of a product to be traced from its raw materials to its final destination in the event of unexpected difficulties is required.

QC testing

Quality control (QC) testing ensures drug safety, efficacy, and effectiveness. It involves specific instruments to ensure the quality of drug testing as per set guidelines. Some of the testing procedures are as follows: friability, weight variation test, disintegration test, dissolution test, and drug assay. The equipment used are as follows: friabilator, electronic weighing balance, mixer, ultraviolet (UV)- visible spectrophotometer, digital pH meter, dissolution test apparatus, and disintegration test apparatus [7-8]. Friability tests the content uniformity and weight variation. It involves the tendency of the tablet to fragment, powder, or chip, which could affect the appearance and uniformity of the drug, while weight variation involves drug distribution uniformity. The weight variation test is applicable when the drug substance is more than 50 mg or 50% by weight of the tablet. The disintegration test involves the time required to break tablet components into particles. It also involves a 10-mesh screen and time is measured while disintegrated particles pass through the mesh screen. The bioavailability of the drug is measured through a dissolution test. It refers to the amount of drug that goes into a solution as per unit time under standardized conditions [8]. The drug assay investigates in vitro quality control testing. It measures and determines the quantity and quality of the specified analyte using the UV-visible spectrophotometer through the amount of radiation absorbed. It also includes the Beer-Lambert law, which relates to the attenuation of light and the properties of the material through which it is passing. Overall, it is important to maintain the quality of a product by performing various quality control (QC) testing upon it to make sure that it is safe for the public domain. At the same time, it maintains the efficiency and quality of the overall product. QC testing also ensures that the drug adheres to the details as per the description and data stated on the drug label. It involves checking the purities and impurities in a drug, active ingredients, drug absorption by the body, etc. The in vitro testing performed in this research determines the quality, efficacy, and effectiveness of diclofenac sodium drug as per United States Pharmacopeia (USP) and British Pharmacopeia.

Quality assurance

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. Quality assurance personnel must establish control or checkpoints to monitor the quality of the product as it is processed and upon completion of manufacture. These begin with raw materials and components 2 testing and include in process, packaging, labeling, and finished product testing as well as batch auditing and stability monitoring.

Sources of quality variation:

Because of the increasing complexity of modern pharmaceutical manufacture arising from a variety of unique drugs and dosage forms, complex ethical, legal and economic responsibilities have been placed on those factors is the responsibility of all those involved in the development, manufacture, control and marketing of quality products. A systematic effective quality assurance program takes into consideration potential raw materials, manufacturing process, packaging material, labeling and finished product variables [1]. For example, for parenteral products which should be sterile and isotonic, a number of quality control tests have been used such as:

Checking the bulk solution for filling, drug content, pH, color, clarity and completeness of solution.

Checking the filled volume of liquids or filled weight of sterile powder for injection in final container at determined intervals during filling.

Testing for leakage from flame-sealed ampoules.

Subject the product to physical examination (visually or mechanically) for appearance, clarity and particulate contamination.
Examining the sterility indicator placed in various areas of sterilizer for each sterilization operation.
Submitting the product for sterility testing other predetermined biological tests to establish the safety and other parameters of the product. On the other hand, the standard quality controls tests that can be used for solid dosage direct compression tablets are:
Checking the weight variation of tablets at predetermined intervals during manufacturing.
Checking the disintegration and/or dissolution time, hardness and friability of the tablets at least during the beginning, middle and end of production or at prescribed intervals during manufacturing.
Testing soluble tablets for compliance with solution time requirements.
Examining products by line inspection or other equally suitable means and removing the defective units prior to packaging.

AIM:
The aim of the study was performed to evaluate the quality of two different brands of Diclofenac and Paracetamol in combination tablets from different manufacturers.

II.OBJECTIVE

Different diclofenac and Paracetamol brands were explored by testing various parameters according to standard methods. The studied parameters included Physical Examination (shape, colour, odour & surface texture), weight variation, friability, disintegration, dissolution and assay. The limits of the official test were referenced from official guidelines of Indian Pharmacopoeia (IP). All brands were tested according to their pharmacopoeial claim and methods for these tests were successfully conducted to find out their qualities. Those methods were economic and authentic. The results and findings of the present study will be interpreted and discussed.

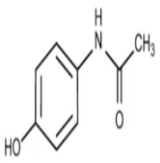
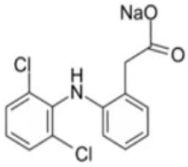
PLAN OF THE WORK
Procurement of Different brands of diclofenac and paracetamol from market
Evaluation parameters
General appearance:

- Size
- Shape
- Colour
- Odour
- surface texture

Dimensional Parameters :

- Thickness
- Diameter
- Weight variation
- Hardness
- Friability
- Disintegration
- Dissolution
- Pharmacopoeial assay

III.DRUG PROFILE

PARAMETERS	PARACETAMOL	DICLOFENAC SODIUM
STRUCTURE		
MOLECULAR FORMULA	C8H9NO2	C14H10CL2NNAO2
MOLAR MASS	151.163g/mol	318.1g/mol
MELTING POINT	169-171ºC	275-277ºC
CAS ID	103-90-2	15307-79-6
IUPAC NAME	N-(4-hydroxyphenyl) acetamide, N-(4-hydroxyphenyl) ethanamide	Sodium;2-(2-(2,6-dichloroanilino) phenyl) acetate
BOILING POINT	420ºC	412ºC
SOLUBILITY	Soluble in acetone, water, alcohol	soluble in methanol, ethanol.
USES	Analgesic and anti-pyretic	Analgesic

PARACETAMOL

It (acetaminophen) belongs to the NSAIDs family. It is widely used and well known by Iraqi population for headache relief and its antipyretic effects. It available as over the counter drug (OTC) and it is available in different dosage forms and different strengths.

Medical uses

Paracetamol is commonly used as analgesic and antipyretic in the treatment fever and as well used to reduce from mild to moderate pain. It has weak anti-inflammatory effects. Generally, it can be used to treat several conditions such as headache, muscle ache, fever and cold, arthritis, backache, toothache. It combined with opioid pain is also used for severe pain such as cancer pain and pain after surgery.

Pharmacokinetics

The bioavailability of paracetamol is about 63-89% and its protein binding of it 10- 25%. Its metabolism is predominantly in the liver and its urinary excretion is about 85-90% after administration.

Side effects

Usual side effects are nausea, vomiting, dark urine, yellowish skin, loss of appetite and stomach pain. Paracetamol toxicity may cause liver damage and skin reactions.

Dose and dosage forms

The commercially available dosage form of paracetamol includes tablets, caplets, capsules, effervescent tablets, suppositories, suspensions, parenteral injections, chewable tablets, oral drops, syrups, elixirs and extended release tablets. The recommended doses of paracetamol in different age groups are listed below.

*The recommended doses of paracetamol based on age of patients.

DICLOFENAC SODIUM

Diclofenac sodium is a non-steroidal anti-inflammatory drug (NSAID), which is used for inflammation, joint stiffness, and rheumatic and non-rheumatic conditions. It has a potentially short half-life (approx 2 hours) and the drug can be administered orally, rectally, or intramuscularly.

Characteristics of diclofenac sodium

It belongs to the class of NSAIDs class, which is solid at room temperature. It appears as white colored crystals and possesses both analgesic and antipyretic properties. It is prescribed to treat pain, ankylosing spondylitis, actinic keratosis, osteoarthritis, ocular inflammation, etc. The mode of action depends upon leukocyte migration inhibition, cyclooxygenase (COX1 & COX2) inhibition, and prostaglandin synthesis inhibition. It also dissipates heat, causing peripheral dilation with increased cutaneous blood flow. In terms of absorption, 50% of the drug reaches the systemic circulation as it undergoes first-pass metabolism. The time taken to reach the maximum concentration is 5.3 hours. The volume distribution (V/F) is 1.4 L/kg. The drug is primarily bound to albumin (99%) and the biological half-life of the drug is one to two hours. The dissociation constant pKa of the drug is 4.15 and water solubility is 2.37 mg/L at 25ºC.

AGE	DAILY DOSE
Adults	2-4 g
2-16 years	0.75-3 g
6-24 months	Up to 20 mg
2-6 months	40-75 mg
Below 2 months	Not recommended

IV.LITERATURE REVIEW

Fatima Ali et.al., According to World Health Organization, the term quality control refers to the sum of all procedures undertaken to ensure the identity and purity of a particular pharmaceutical. Quality control is an essential operation of the pharmaceutical industry. In addition to the apparent features of tablets, tablets must meet other physical specifications and quality standards. These include criteria for weight, weight variation, content uniformity, thickness, hardness, disintegration, and dissolution. Thus in this project, five types of paracetamol tablets from different companies which are widely used in the private pharmacies in Hilla city were subjected to quality control tests to indicate whether these products will fit to the standard criteria of the United States Pharmacopeia or not. The data indicated that all brands succeeded to pass most quality control tests with some exceptions.

Huma Dilshad et.al., Acetaminophen is used analgesic and available in several brands in the market which

makes it difficult to select the safe and effective one. There for The aim of study to establish pharmaceutical equivalence of the different brands of acetaminophen tablets available in Karachi, Pakistan. Four different brands of acetaminophen tablets (500 mg) were included in study. The quality control parameters which are studied are weight variation test, hardness test, thickness, friability, disintegration and dissolution specified by BP/USP (British and United state Pharmacopoeia). Weight variation and hardness value requirement was compiled by all brands. Disintegration time for all brands was within 15 minutes also complying the BP/USP recommendation. All brands showed more than 80 % drug release within 45 minutes. The present findings suggest that almost all the brands of acetaminophen that are available in Karachi meet the BP/USP specification for quality control analysis.

Safila Naveed *et.al.,* Diclofenac potassium is a non-steroidal anti-inflammatory drug and a prostaglandin (PG) synthetase inhibitor. The objective of this study was to develop a spectrophotometric method for the assay of diclofenac potassium. A series of diclofenac potassium solutions were prepared ranging from 200 ppm to 12.5 ppm. After preparation of a standard stock solution of 200 ppm in 100 ml of water, different dilutions were made (100ppm, 50ppm, 25ppm and 12.5ppm). At the wavelength 242nm, the absorbance of the standard preparation and dilutions was measured using a UV spectrophotometer. In this study a precise and accurate method was developed. The validation of the developed method for the assay of diclofenac potassium was done by various parameters that included linearity, accuracy test and precision. The method showed good reproducibility and good recovery with % RSD less than 2. The method was found to be simple, economical, rapid, specific, precise and accurate.

Mahmoud M. Sebaiy *et.al*., Early treatment of pain is of a great importance as unrelieved pain can have profound psychological effects on the patient, and acute pain that is poorly managed initially can degenerate into chronic pain, which may prove to be much more difficult to treat. It is important to assess and treat the mental and emotional aspects of the pain as well as its physical aspects. Although drug therapy is a mainstay of pain treatment, physical methods such as physiotherapy (including massage and the application of heat and cold), surgery, and drug monitoring are also very valuable. In this review article, we will shed the light on different ways of some analgesic drugs monitoring and analysis using different techniques in addition to the most recommended combinations of our cited drugs for pain relief.

Madan mohan gupta *et.al*., The objective of this study is to conduct in-vitro quality control testing of diclofenac sodium tablets involves weight variation test, drug assay, friability test, and the disintegration and dissolution test. Two brands of diclofenac sodium tablets were used in the study, named Brand A and Brand B. Quality control (QC) test results for diclofenac sodium tablets show that both Brand A and Brand B conform to the United States Pharmacopeia (USP) standards. In terms of weight variation, Brand A and B have an above the mean weight limit variation of 2.79% and 2.05%, respectively. The lower mean weight limit variations are 1.21% and 1.27%, respectively, which are within the 10% standard limits of USP. Friability tests show that Brands A and B have an average friability of 0.062% and 0.01% mass loss, which are within the 1% mass loss limits of USP. In terms of drug assay, both Brands A and B fall under the USP parameter of 85%-115%, respectively. The disintegration test shows that Brand A and Brand B fall within a 15-minute time interval segment with disintegration time calculated as 6.69 min and 7.02 min for Brands A and B, respectively. Brand B of Diclofenac Sodium has a drug dissolution percentage of 90.7% within a 45-min sampling time interval. Brands A and B pass the pharmacopeia limits set under the USP standards. The friability test shows that the loss of mass for both Brands A and B was within the 1% standard limit. Similarly, with regard to weight variation, both brands conform under the normal limit of 10% above or lower the mean weight. In terms of drug assay, both brands' drug availability was within the specified 85%-115% standard range. They passed the disintegration and dissolution test within a time limit of less than 15 minutes and 45 minutes, respectively.

Tania Sultana *et.al*., The aim of this study is to determine the potency of drug available in our market in Bangladesh. Diclofenac Sodium is a potent Non-Steroidal Anti-Inflammatory Drug (NSAID) and that are widely used and it is an Over the Counter (OTC)

drug in Bangladesh. Potency determination was performed to evaluate that the marketed sample comply with the declared specification or not. In vitro Dissolution study was performed to see that if potency is high but the drug is not bioavailable. Hardness is also checked to see that whether it interfere with the dissolution which ultimately effect the bioavailability. In this present study a simple, cost effective and spectrophotometric method for the potency determination of marketed Diclofenac Sodium tablets is used. Four samples were randomly collected from the market and coded as D01, D02, D03 and D04 and the potency determined are 99.30%, 103.38%, 98.22% and 102.16% respectively. Hardness and in vitro dissolution of the above four brands of Diclofenac Sodium tablets were also studied and reported in the paper. After 1 h Dissolution release of DO1, D02, D03 and D04 are 94.16%, 93.97%, 96.94% and 98.5% respectively. From all of the studies it seems that the samples were collected complies with the BP and USP requirements.

Peeyush Yadav *et.al*., A properly designed system will provide a high degree of assurance that every step, process, and change has been properly evaluated before its implementation. Validation is an important step carried out in order to control the entire process, and the process adapted to produce itself must assure that process will consistently produce the expected results and maintain the desired quality of the final product. Process validation is the validation of each and every step of the processes which involves series of activities carried out in order to have the assurance of the products manufactured. Each and every step should be scientifically planned, conducted and documented appropriately and for this one should have sound knowledge and understanding regarding the process as well as the product. So, the study here shows the research work done on the formulation and process validation of diclofenac sodium and paracetamol combination tablet, the critical process parameters involved in the manufacturing process and the consistency in the results of the three consecutive batches.

A. R. Umarkar *et.al*., A new simple, specific, precise and accurate multicomponent method has been developed for simultaneous estimation of Famotidine (FAM) and Diclofenac potassium(DICP) in tablet formulation. The detection of the constituents was done using UV detector at 260, 270, 275, 280 and 290 nm for FAM and DICP. Recovery, study values of FAM and DICP is 100.04±0.34 and 99.98±0.27 respectively, relative standard deviation of less than 2% for the assay and linearity coefficient of 0.9998 that the method is precise, accurate and linear in the concentration given and demonstrated the method developed is rugged. Liner response obtained for FAM was in the concentration range 2.-10µg/mL and DICP in the range 5-25 µg/mL.

P.Vasubabu *et.al.,*A simple, rapid, accurate, precise, and economic spectrophotometric method for simultaneous estimation of paracetamol and diclofenac in tablet dosage form have been developed and validated. Paracetamol and diclofenac show absorbance maximums at 242 and 273nm respectively by using 6.8 phosphate buffers, so absorbance was measured at the same wave lengths for the estimation of paracetamol and diclofenac. Absorbance is measured at 240.2 nm (Isoabsorptive point) and 258.4nm (λmax of diclofenac). Both drugs obey the Beer's Lambert's law in the concentration range of 10-30 µg/mL. Methods are validated according to ICH guidelines and can be adopted for the routine analysis of paracetamol and diclofenac in tablet dosage form.

Mali Audumbar Digambar *et.al.,* A simple, precise, accurate and economical UV visible spectrophotometric method has been developed for estimation of Diclofenac sodium drug by AUC method. The standard and sample solutions were prepared by using double distilled water as a solvent. Quantitative determination of the drug was performed at wavelength range 270-282 nm. The linearity was established over the concentration range of 05, 10, 15, 20 & 25 µg/ml for Diclofenac sodium with correlation coefficient value of 0.9981. Precision studies showed that % relative standard deviation was within range of acceptable limits. The mean percentage recovery was found to be 99.38%.The proposed method has been validated as per ICH guidelines.

Siladitya Behera et.al.,A novel,safe and sensitive method of spectrophotometric estimation in UV-region has been developed for the assay of Paracetamol in its tablet formulation. The method have been developed and validated for the assay of Paracetamol using Methanol and water as diluents. Which does not shows

any interference in spectrophotometric estimations. All the parameters of the analysis were chosen according to ICH [Q2(R1)] guideline and validated statistically using RSD and %RSD along with neat chromate grams.

Abdullah Al Ragib *et.al*., Diclofenac Sodium is a type of non-steroidal anti-inflammatory drug which is established to treat different symptoms by lessens the substances in the body that cause the pain and swelling to occur. The study was assessed to find out the physicochemical parameters of different brands of diclofenac sodium tablets in Bangladesh to comply them mostly with the standard parameters of BP/USP specifications. The tablets present in the market of different popular brands were chosen for the study of different quality control test like physical appearance, hardness, friability, disintegration time, weight variation, dissolution rate & potency were evaluated. The observed hardness results were shown not more than 4-10 kg-ft. and the friability results were also shown not more than 1 % that matched the BP/USP specification. According to in vitro dissolution of pharmacopeia, Megafen (73.82%) and A-fenac (68.61%) dissolution profile didn't match with the standard limit. Potency tests were also done by following standard protocol in which all brands met with the standard. This study is expected to be a point of appreciation in constructing consciousness between population and prescriber communities to have the greater surplus of medicines by choosing the appropriate products among different commercial brands.

V.MATERIALS AND METHODS

Materials

QC testing of the paracetamol & diclofenac sodium drug involves the following equipment: electronic weighing balance (Adam AFA-120LC, Adam Equipment, Milton Keynes, UK), UV visible spectrophotometer (Agilent 8453; Agilent Technologies, Santa Clara, California), mixer (Maxi Mix II), digital pH meter (OAKTON Instruments, Vernon Hills, IL), friabilator (Electro lab EF2, Electro lab India Pvt. Ltd., Mumbai, India), dissolution test apparatus (Electro lab EDT O8Lx; Electro lab India Pvt. Ltd.), and disintegration test apparatus (Electro lab ED 2L; Electro lab India Pvt. Ltd.). Some of the materials used in the in-vitro QC test are as follows: diclofenac sodium pure drug (Sigma-Aldrich, St. Louis, Missouri), commonly available paracetamol & diclofenac sodium tablets (Brand A and Brand B) conventional, Tulsion-412 (cholestyramine resins manufactured by Cadila Pharmaceuticals, Ahmedabad, India), sodium hydroxide, potassium dihydrogen phosphate, and distilled water (pharmaceutical grade). The tests performed with the equipment mentioned above are as follows: friability, disintegration test, weight variation test, drug assay, and dissolution test, physical examination.

Methods

Physical examination

Ten tablets where removed from the sheet and carefully examined by naked eye to detect its physical properties (appearance, color, break line, any cracked edges or any deformations), the process was repeatedly performed for each type of paracetamol &diclofenac combination tablet from different companies.

Weight variation test

This test examines uniformity in accordance with the formulation of each batch of tablets, which illustrates its content. In this study, we selected 20 tablets of paracetamol& diclofenac sodium from Brand A. which were weighed individually and collectively. Weight variation was calculated using the formula - (Initial weight - Average weight)/Average weight X 100. It is meant to compare the USP limits and the data were recorded in table format. The same procedure was repeated for Brand B.

Size variation test

Ten tablets were removed from the sheet and each tablet was placed in digital caliper (WEILIANG Co.China) to measure its height. The steps were 7 repeated the rest of the tablets and then mean and standard deviation were calculated and compared with the accepted ±5% value .

Disintegration test

As per USP standards, the paracetamol & diclofenac sodium tablets are disintegrated into small granules to increase the surface area. It involves the disintegration of the tablets in a liquid medium as stated in the monograph under experimental conditions and recorded as disintegration time. The test is crucial, as it provides critical safety data in regard to the bioavailability of the solid dosage form of the drug. During this test, six tablets from Brand A were randomly selected and one tablet was placed in each test tube with a mesh size of 10 basket as per USP standards. The basket was placed in a 1 liter beaker containing phosphate buffer solution of pH 6.8 at 37°C. The apparatus was stirred at 28-32 cycles/minutes and, simultaneously, a stopwatch was started. When all the particles passed from each test tube into the beaker, the finishing time was noted as the disintegration time. The same procedure was repeated for Brand B. This disintegration test was a quantitative test, as time was measured during the test.

Friability test

Friability is the tendency of tablet to powder, chip or fragment and this can affect the elegance, appearance and the consumer acceptance of the tablet, and also added to tablet's weight variation or content uniformity problem. We used tablet friability tester (GUOMING CS-2 / China), to measure friability of the different brand of paracetamol and diclofenac tablet. The weight of 10 tablets of each brand of paracetamol and diclofenac where measured and the tablets were loaded in the friability tester. The apparatus exposed tablets to rolling and repeated shocks as they fall 6 inches in each turn within apparatus. After 48 minutes of 100 cycles, the tablets were removed from the device, brushed to remove any powders and weighed again. The percentage of weight loss (Friability %) was calculated according to the following equation brand of paracetamol tablet.

$$Friability\ \% = \frac{W_{initial} - W_{final}}{W_{initial}} \times 100\%$$

Where Wi is the initial weight and Wf is final weight Friability values more than 5% were consideredas unacceptable based on the USP.

FRIABILITY TESTER

As per USP standards, the friability test was performed using the Roche friabilator [6]. It checks the tendency of the tablet to crumble, chip, or break upon abrasion or compression. It is important to check the friability of a tablet for complete dissolution in the gastrointestinal tract. The test checks the sturdiness of a tablet, and a loss of 1% tablet mass is acceptable during the process.

Hardness test

Hardness test (crushing strength) is the load required to crushing the tablet when placed on its edge. Hardness is the force required to break the tablet by diametric compression tester. Usually, tablet hardness tester is a portable semi-automatic electronic tablet hardness tester designed to accept tablet up to 30 mm in diameter. Unfortunately, in our project, such device was not available, and a manual hardness tester was used to perform this test. The hardness of ten tablets was measured by placing 1 tablet each time in the hardness tester (Campbel electronics \ China), and

recorded the force required to break or crack the tablet. The mean and standard deviation of the hardness were calculated and compared between different paracetamol brands. Based on the USP, conventional tablet hardness should range between 2.5 to 10 kg/cm2. Values outside this range were considered unaccepted results.

PFIZER HARDNESS TESTER

Dissolution test

The dissolution test is crucial to ensure the therapeutic effectiveness of a drug and its bioavailability. It measures the extent of solution formation. In this test, we required a 10L phosphate buffer at pH 6.8.The following formula was used as a basis for preparing the buffer - 6.8 g KH_2PO_4 + 0.94 g NaOH dissolved in 1L of distilled water gives a phosphate buffer of pH 6.8.In order to prepare a 10L buffer solution, the following ingredients were used - 68 g of KH_2PO_4 and 9.4g of NaOH were dissolved in 0.5L distilled water in a 1L volumetric flask. The flask was shaken to form a solution. The same procedure was repeated to expand the solution to make a 10L buffer using distilled water. In order to attain 6.8 pH for the buffer, HCl and NaOH were used accordingly to adjust the pH. The following equipment was used for the dissolution test - Electrolab EDT (Electrolab India Pvt. Ltd.) - 08Lx Type 2. A type 2 dissolution instrument was used because as per the monograph of the tablet, a paddle (Type 2) instrument is used for the dissolution study of the tablet. This test provides us a correlation between in vitro and in vivo along with the efficacy of the dosage form. The dissolution beaker was filled with 900 ml of phosphate buffer at 6.8 pH and heated to 37±0.5°C. One tablet from Brand A was added to each beaker and stirred at 75 rpm.At specific time intervals - 5, 10, 15, 30, 45, 60, and 75 min, respectively, 5 ml of the solution was removed and 5 ml of the buffer solution was added. The absorbance of diclofenac sodium was determined using UV visible spectrophotometer at the above-mentioned time intervals.

DISSOLUTION APPARATUS

VI.RESULTS AND DISCUSSION

According to World Health Organization (WHO), the term quality control refers to the sum of all procedures undertaken to ensure the identity and purity of a particular pharmaceutical. Quality control is an essential operation of the pharmaceutical industry. Drugs must be marketed as safe and therapeutically active formulations whose performance is consistent and predictable. It not only protects the manufacturer against compensation claims, but also guarantees the patient a safe and effective product. Thus, in addition to the apparent features of tablets, tablets must meet other physical specifications and quality standards. These include criteria for weight, weight variation, content uniformity, thickness, hardness, disintegration, and dissolution. These factors must be controlled during production (in-process controls) and verified after the production of each batch to ensure that established product quality standards are met.

Physical examination

The various types of diclofenac and paracetamol tablets were subjected to physical examination using naked eye. The parameter like shape, colour, odour and surface texture were investigated and the results are listed in Table 4.1.

Sample	Shape	Colour	Odour	Surface Texture
A	Rectangular	white	odourless	Smooth
B	Rectangular	white	odourless	Smooth

Weight variation test

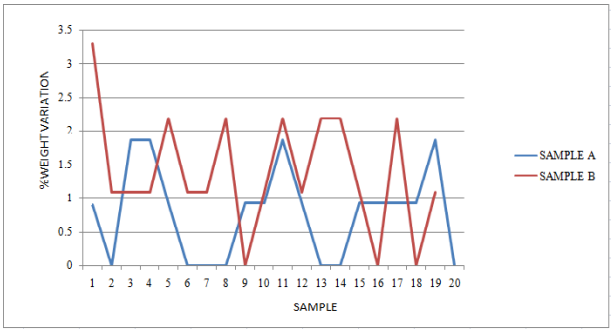
Take a 20 tablets and individual tablet weight weigh accurately in weight balance and note down the each tablet weight and calculate the average weight and weight variation of each tablets. Compare the weight variation of two brand tablet.

Weight variation = average weight – individual weight of the tablet

Percentage weight variation = weight variation /average ×100

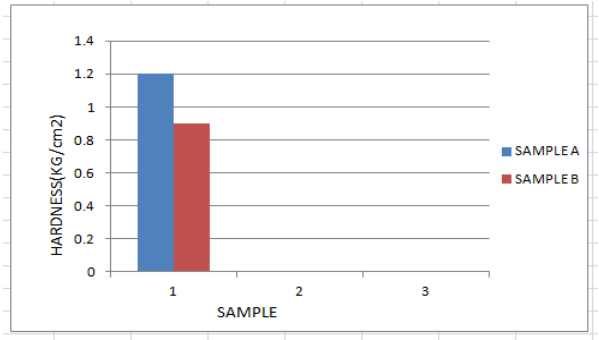
S.NO	SAMPLE-A (kg/cm^2)	SAMPLE-B (kg/cm^2)
1.	1.2	0.9
2.	1	0.9
3.	1.4	0.8
AVERAGE	1.2	0.9

S.no	Sample – A		Sample –B	
	Average weight of Tablets = 1.07g		Average weight of Tablet = 0.91g	
	Weight of individual Tablets [g]	% Deviation	Weight of individual Tablets [g]	% Deviation
1	1.06	0.9	0.91	0
2	1.07	0	0.94	3.29
3	1.09	1.86	0.92	1.09
4	1.05	1.86	0.92	1.09
5	1.08	0.93	0.90	1.09
6	1.07	0	0.93	2.19
7	1.07	0	0.92	1.09
8	1.07	0	0.92	1.09
9	1.08	0.93	0.93	2.19
10	1.06	0.93	0.91	0
11	1.09	1.86	0.92	1.09
12	1.08	0.93	0.89	2.19
13	1.07	0	0.90	1.09
14	1.07	0	0.93	2.19
15	1.06	0.93	0.89	2.19
16	1.08	0.93	0.90	1.09
17	1.08	0.93	0.91	0
18	1.08	0.93	0.92	2.19
19	1.09	1.86	0.91	0
20	1.07	0	0.90	1.09



HARDNESS TEST:

To take a tablets and fix tablets between the piston and bolt and compress the tablets between a holding anvil and a piston connected to a force reading gauge when its plier – like handles are gripped. The point where tablets gets break down, it is noted by reading gauge.



Hardness variation between two brand of sample

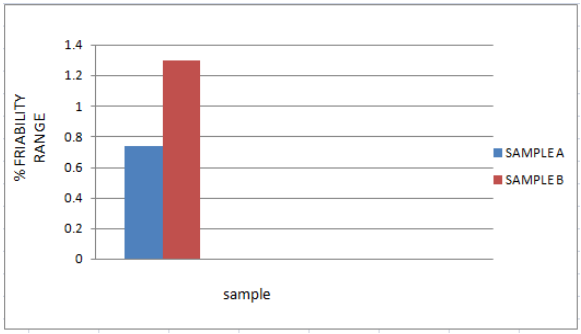
FRIABILITY TEST:

Take five tablets and take initial weight of it and put it into friabilator. Now rotate the down at 25rpm per min for 10mins.During this tablets gets dropped on plastic from 6 inches, it will pass through mechanical shocks. After 10 minutes, calculate final weight of tablets and the percentage friability can be calculated.

% Friability = W 1-W2/W1x100

W1= Weight of tablets before testing

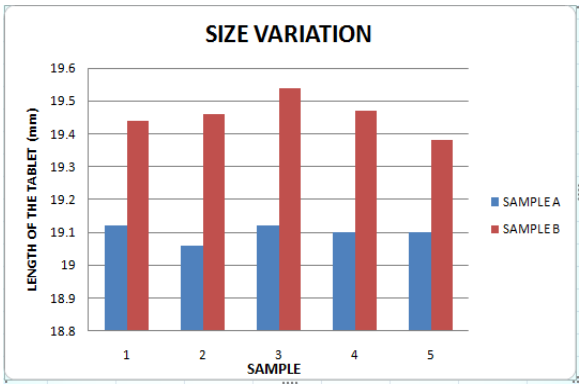
W2= Weight of tablets after testing



Friability variation between two brand of sample

SIZE VARIATION TEST

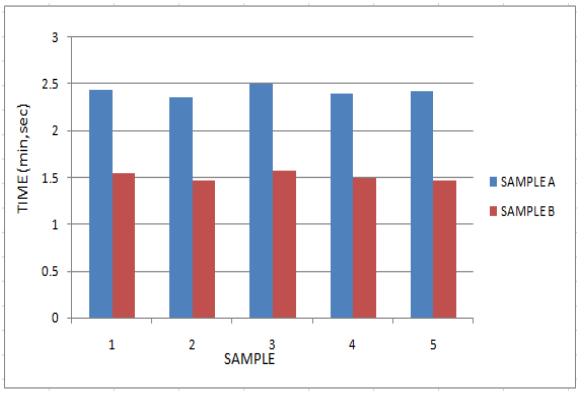
S.NO	SAMPLE A			SAMPLE B		
	LENGTH (mm)	THICKNESS (mm)	WIDTH (mm)	LENGTH (mm)	THICKNESS (mm)	WIDTH (mm)
1	19.12	6.31	8.88	19.44	6.47	9.18
2	19.06	6.33	8.89	19.46	6.31	9.24
3	19.12	6.34	8.87	19.54	6.43	9.19
4	19.10	6.30	8.89	19.47	6.48	9.20
5	19.10	6.30	8.86	19.38	6.41	9.20
AVG	19.10	6.31	8.87	19.45	6.42	9.20



Size variation between two brand of sample

DISINTEGRATION TEST

DISINTEGRATION TIME (min)		
S.NO	SAMPLE - A	SAMPLE - B
	2.44	1.55
	2.36	1.47
	2.50	1.57
	2.40	1.50
	2.43	1.47
AVG	2.42	1.51

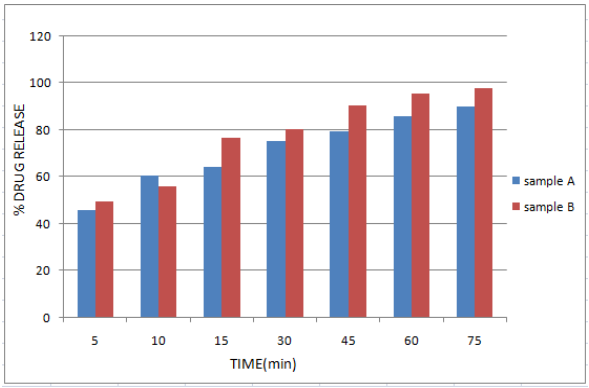


Disintegration time(min) between two brand of sample

VII.DISSOLUTION TEST

As per test results a Brand A tablet releases 83.003% drug in 45 minutes while a Brand B tablet releases 90.74% in the same time period. The variation in test results for Brand A can be due to random errors in measurement while using lab instruments or while using UV visible spectroscopy. The data provided indicated that both brands of diclofenac sodium were dissolved at a fast rate then, as shown in the graph, the percentage of drug released by Brand A increased during a shorter period of time than its peak rate of dissolution, whereby it continued slowly until almost all the drug was released and the same can be observed for Brand B as well. Both brands exhibited almost similar rates of release of the drug over a period of time.

SAMPLING TIME (min)	SAMPLE-A (%DRUG RELEASE)	SAMPLE-B (%DRUG RELEASE)
5	45.60	49.24
10	60.45	55.69
15	62.70	76.53
30	75.06	80.09
45	78.86	89.89
60	85.39	95.13
75	89.70	97.65

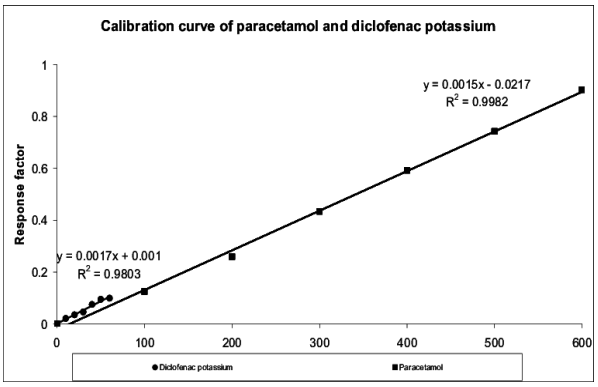


Dissolution time variation between two brand of sample

Analysis of formulation

A drug assay is crucial, as it validates the drug as per the labeled amount. It checks the dosage formulation as per the desired formulation based upon precision, accuracy, robustness, and selectivity. In this study,50 mg diclofenac sodium and 325mg of paracetamol tablet in combination were selected and crushed into a powder. The crushed powdered drug which is equivalent to 0.32g of Paracetamol and 0.05g of diclofenac sodium was transferred to 100ml volumetric

flask and completely dissolved in methanol. The process was performed using the instrument Maxi Mix II, which also maintained the uniformity of the mixture . The contents were made up and divided into 100 ml using a volumetric flask and 10 ml of the solution was pipetted and diluted to 100 ml, which was placed in the UV visible spectrophotometer. The wavelength of absorbance of the spectrophotometer was set to 278 nm max.



VIII.SUMMARY &CONCLUSION

According to World Health Organization, the term quality control refers to the sum of all procedures undertaken to ensure the identity and purity of a particular pharmaceutical. Quality control is an essential operation of the pharmaceutical industry. In addition to the apparent features of tablets, tablets must meet other physical specifications and quality standards. These include criteria for weight, weight variation, content uniformity, thickness, hardness, disintegration, dissolution & Pharmacopeial assay. Thus in this project, Two types of diclofenac sodium and paracetamol tablets from different companies were subjected to quality control tests to indicate whether these products will fit to the standard criteria of the Indian Pharmacopeia or not. The data indicated that all brands succeeded to pass most quality control tests with some exceptions.

Paracetamol is a well established and proven analgesic and antipyretic drug, diclofenac for anti inflammatory and pain killer. Therapeutic response of any formulation depends on its quality parameters. From the study it was identified that weight variation and friability test of both brands complied the specification. Variation was obtained in hardness, disintegration time and dissolution profile during the test procedure. It should be strictly considered that an ideal tablet will have sufficient hardness to maintain its mechanical stability but not more. Because harder tablet can delay disintegration time or alter dissolution profile. Finally, as quality control parameters are related to one another from initial step to pharmacological action of the drug.

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