University of Basrah

College of Pharmacy

Evaluation of Tablet Dosage Form

By:

Nabaa Muhammed Abed

Hanaa Abdulreda

5th year graduation project

This project is submitted to the department of pharmaceutics as a partial fulfilment for graduation in college of pharmacy

Supervised by:

Dr. Mohammed Sattar

Table of Contents

1 Introduction

Tablets are solid dosage forms usually prepared with the aid of suitable pharmaceutical excipients. They may vary in size, shape, weight, hardness, thickness, disintegration, and dissolution characteristics and in other aspects, depending on their intended use and method of manufacture. Most tablets are used in the oral administration of drugs. Many of these are prepared with colorants and coatings of various types. Other tablets, such as those administered sublingually, buccally, or vaginally, are prepared to have features most applicable to their particular route of administration. Tablets are prepared primarily by compression, with a limited number prepared by molding. Compressed tablets are manufactured with tablet machines capable of exerting great pressure in compacting the powdered or granulated material. Their shape and dimensions are determined by the use of various shaped punches and dies. Molded tablets are prepared on a large scale by tablet machinery or on a small scale by manually forcing dampened powder material into a mold from which the formed tablet is then ejected and allowed to dry. Some tablets are scored, or grooved, which allows them to be easily broken into two or more parts. This enables the patient to swallow smaller portions as may be desired, or when prescribed, it allows the tablet to be taken in reduced or divided dosage. Some tablets that are not scored are not intended to be broken or cut by the patient since they may have special coatings and/or drug release features that would be compromised by altering the tablet's physical integrity [1].

2 Advantages

1. The oral route represents a convenient and safe way of drug administration [2].
2. The preparation procedure enables accurate dosing of the drug [2].

3. They are a unit dose form, and they offer the greatest capabilities of all oral dosage forms for the greatest dose precision and the least content variability [3].
4. Their cost is lowest of all oral dosage forms [3].
5. They are the lightest and most compact of all oral dosage forms [3].
6. They are in general the easiest and cheapest to package and ship of all oral dosage forms [3].
7. Product identification is potentially the simplest and cheapest, requiring no additional processing steps when employing an embossed or monogrammed punch face [3].
8. They may provide the greatest ease of swallowing with the least tendency for "hang-up" above the stomach, especially when coated, provided that tablet disintegration is not excessively rapid [3].
9. They lend themselves to certain special release profile products, such as enteric or delayed-release products [3].
10. They are better suited to large-scale production than other unit oral forms [3].
11. They have the best combined properties of chemical, mechanical and microbiologic stability of all the oral forms [3].

3 Disadvantages

1. The main disadvantage of tablets as a dosage form is the problem of poor bioavailability of drugs due to unfavorable drug properties, e.g. poor solubility, poor absorption properties and instability in the gastrointestinal tract [2] .
2. Some drugs may cause local irritant effects or otherwise cause harm to the gastrointestinal mucosa [3].

3. Some drugs resist compression into dense compacts, owing to their amorphous nature or flocculent, low-density character [3].
4. Bitter-tasting drugs, drugs with an objectionable odor, or drugs that are sensitive to oxygen or atmospheric moisture may require encapsulation or entrapment prior to compression (if feasible or practical), or the tablets may require coating. In such cases, the capsule may offer the best and lowest cost approach [3].

4 Evaluation

To design tablets and later monitor tablet production quality, quantitative evaluations and assessments of a tablet's chemical, physical, and bioavailability properties must be made. Not only could all three property classes have a significant stability profile, but the stability profiles may be interrelated, i.e., chemical breakdown or interactions between tablet components may alter physical tablet properties, gready changing the bioavailability of a tablet system [3].

In tablet formulation development and during manufacturing of tablets, a number of procedures are used to assess the quality of the tablets. Some test methods are described in pharmacopoeias and these tests are traditionally concerned with the content and the in vitro release of the active ingredient. Test methods not described in pharmacopoeias are sometimes referred to as non-compendial and concern a variety of quality attributes that need to be evaluated, such as the porosity of tablets [2]. The methods of tablet assessment generally classified into non-official (or non-pharmacopeial) tests and official (or pharmacopeial) tests

4.1 Non-official test:

4.1.1 General Appearance [3]:

General Appearance. The general appearance of a tablet, its visual identity and overall ''elegance" is essential for consumer acceptance, for control of lot-to-lot uniformity and general tablet-to-tablet uniformity, and for monitoring trouble-free manufacturing. The control of the general appearance of a tablet involves the measurement of a number of attributes such as a tablet's size, shape, color, presence or absence of an odor, taste, surface texture, physical flaws and consistency, and legibility of any identifying markings

4.1.1.1 Size and Shape

The size and shape of the tablet can be dimensionally described, monitored, and controlled. A compressed tablet's shape and dimensions are determined by the tooling during the compression process. The thickness of a tablet is the only dimensional variable related to the process. At a constant compressive load, tablet thickness varies with changes in die fill, with particle size distribution and packing of the particle mix being compressed, and with tablet weight, while with a I constant die fill, thickness varies with variations in compressive load. Tablet thickness is consistent batch to batch or within a batch only if the tablet granulation or powder blend is adequately ^ consistent in particle size and size distribution, if the punch tooling is of consistent length, and if the tablet press is clean and in good working order. The crown thickness of individual tablets may be measured with a micrometer, which permits accurate measurements and provides information on the variation between tablets. Other techniques employed in production control involve placing 5 or 10 tablets in a holding tray, where their total crown thickness may be measured with a sliding caliper scale. This method is much more rapid than measurement with a micrometer in providing an overall estimate of tablet thickness in production operations, but it does not as

readily provide information on variability between tablets; however, if the punch and die tooling has been satisfactorily standardized and the tablet machine is functioning properly, this method is satisfactory for production work. Tablet thickness should be controlled within a ±5% variation of a standard value. Any variation Tn tablet thickness within a particular lot of tablets or between manufacturer's lots should not be apparent to the unaided eye for consumer acceptance of the product. In addition, thickness must be controlled to facilitate packaging. Difficulties may be encountered in the use of unit dose and other types of packaging equipment if the volume of the material being packaged is not consistent. A secondary packaging problem with tablets of variable thickness relates to consistent fill levels of the same product container with a given number of dosage units. The physical dimensions of the tablet, along with the density of the materials in the tablet formulation and their proportions, determine the weight of the tablet. The size and shape of the tablet can also influence the choice of tablet machine to use, the best particle size for the granulation, production lot sizes that can be made, the best type of tablet processing that can be used, packaging operations, and the cost to produce the tablet. The shape of the tablet alone can influence the choice of tablet machine used. Shaped tablets requiring "slotted punches" must be run at slower speeds than are possible with round tablets, using conventional punches. Because of the nonuniform forces involved within a tablet during compression, the more convex the tablet surface, the more likely it is to cause capping problems, forcing the use of a slower tablet machine or one with precompression capabilities.

4.1.1.2 Unique Identification Markings

Pharmaceutical companies manufacturing tablets often use some type of unique markings on the tablet in addition to color, to aid in the rapid identification of their products. These markings utilize some form of embossing, engraving, or printing. A

look into the product identification section of the current Physician's Desk Reference (PDR),7 provides a quick reference to the multitude of marking variations, both artistic and informational, that can be produced. The type of informational markings placed on a tablet usually includes the company name or symbol, a product code such as that from the National Drug Code (NDC) number, the product name, or the product potency. In the future, these identifying marks, in conjunction with a greater diversity of tablet sizes and shapes, may provide the sole means of identification of tablets, if the pharmaceutical industry continues to lose the use of approved Food, Drug, and Cosmetic (FD&C) colors.

4.1.1.3 Organoleptic Properties:

A// Color:

Many pharmaceutical tablets use color as a vital means of rapid identification and consumer acceptance. The color of a product must be uniform within a single tablet (nonuniformity is generally referred to as "mottling"), from tablet to tablet, and from lot to lot. Nonuniformity of coloring not only lacks esthetic appeal but could be associated by the consumer with nonuniformity of content and general poor quality of the product.8 The eye cannot discriminate small differences in color nor can it precisely define color. The eye has limited memory storage capability for color, and the storage of visually acquired data is difficult, which results in people perceiving

the same color differently and a single person describing the same color differently at different times. In addition, visual color comparisons require that a sample be compared against some color standard. Color standards themselves are subject to change with time, thus forcing their frequent redefinition, which can lead to a gradual and significant change in acceptable color. Efforts to quantitate color evaluations have used reflectance spectrophotometry, tristimulus colorimetric measurements, and the use of a micro-reflectance photometer to measure the color uniformity and gloss on a tablet surface.

B// Odor:

The presence of an odor in a batch of tablets could indicate a stability problem, such as the characteristic odor of acetic acid in degrading aspirin tablets^ however, the presence of an odor could be characteristic of the drug, (vitamins have a characteristic odor), added ingredients (flavoring agents have pleasant odors), or the dosage form (film-coated tablets usually have a characteristic odor).

C// Taste:

Taste is important in consumer acceptance of chewable tablets. Many companies utilize taste panels to judge the preference of different flavors and flavor levels in the development of a product. Owing to the subjectiveness of "taste" preference, however, the control of taste in the production of chewable tablets is often simply the presence or absence of a specified taste

D// Appearance:

Tablets defects and surface roughness (specially for coated types) are also investigated. A tablet's level of flaws such as chips, cracks, contamination from foreign solid substances (e.g., hair, drops of oil, and "dirt"), surface texture ("smooth" versus "rough"), and appearance ("shiny" versus "dull") may have a zero-defect

specification, but the visual inspection techniques used for detecting or evaluating these characteristics are subjective in nature. Electronic devices that are currently being developed hold promise for making inspection a more quantitative and reproducible operation

4.1.2 Hardness test [3]

Tablets require a certain amount of strength, or hardness to withstand mechanical shocks of handling in manufacture, packaging, and shipping. In addition, tablets should be able to withstand reasonable abuse when in thehands of the consumer, such as bouncing about in a woman's purse in a partially filled prescription bottle. the relationship of hardness to tablet disintegration, and perhaps more significantly, to the drug dissolution release rate, has become apparent. The monitoring of tablet hardness is especially important for drug products that possess real or potential bioavailability problems or that are sensitive to altered dissolution release profiles as a function of the compressive force employed.

To perform this test, a tablet is placed between two anvils, force is applied to the anvils, and the crushing strength that just causes the tablet to break is recorded.

Several devices operating to test tablet hardness:

1. Monsanto tester
2. Strong-Cobb tester
3. Pfizer tester
4. Erweka tester
5. Schleuniger tester

Acceptance Criteria

Record the hardness at this point and calculate the average.

i. 4-10kg (1Kg=10 newton) for normal tablet
ii. 3kg for chewable tablets
iii. 10-20Kg for coated tablets

4.1.3 Friability [4]

This test is a method to determine physical strength of uncoated tablets upon exposure to mechanical shock and attrition.

4.1.3.1 Apparatus discrimination

This instrument consists of a plastic chamber for placing the tablets which is attached to a horizontal axis. The drum has an inside diameter of 283 to 291mm USP and is about 36 to 40 mm USP in depth, made of a transparent synthetic polymer with polished internal surface. A set of pre weighed tablets [if one tablet weigh 650mg or less then approx. 6.5g of total weight should be taken and for more than 650mg/tablet weight, 10 tablets should be taken] are placed in the plastic chamber revolving at 24-

25 rpm for 4 min (100 times) USP. The tablets are subjected to combined effects of abrasion and shock. The tablets are dropped at a distance of six inches on each revolution. The tablets are tumbled at each turn of the drum by a curved projection with an inside radius between 75.5 to 85.5 mm (USP) that extends from the middle of the drum to the outer wall. If the tablet size or shape becomes irregular (diameter of tablets is greater than 13mm) adjust the drum so that base forms an angle of about 10 degrees with bench top and the tablets fall freely when drum is rotated.

4.1.3.2 Acceptance Criteria

Conventional compressed tablets that lose less than 0.5% to 1% of weight are considered acceptable. Generally, the test is run once. If obviously cracked cleaved or broken tablets present in the tablet sample after thumbing, the sample fails the test. If the results are doubtful or if the weight loss is greater than the targeted value, the test should be repeated twice and mean of the three tests are determined so the result should be less than 1% of weight loss is considered acceptable for most product. If the tablets were not reaching above criteria those tablets are considered unfit for commercial use placed in the plastic chamber revolving at 24-25rpm for 4 min (100times) USP. The tablets are subjected to combined effects of abrasion and shock. The tablets are dropped at a distance of six inches on each revolution. The tablets are

tumbled at each turn of the drum by a curved projection with an inside radius between 75.5 to 85.5 mm(USP) that extends from the middle of the drum to the outer wall. If the tablet size or shape becomes irregular (diameter of tablets is greater than 13mm) adjust the drum so that base forms an angle of about 10 degrees with bench top and the tablets fall freely when drum is rotated.

4.1.3.3 Special Precautions

1. In case of hygroscopic tablets, a humidity-controlled environment (relative humidity less than 40%) is required for testing.
2. Most effervescent tablets and some chewable tablets undergo high friability weight loss which is an indication for the special stack packing that is required for these types of tablets.
3. friability test is required for tablets even after completing the hardness test because measuring the hardness of a tablet is not a reliable indicator for tablet strength as some formulations when compressed into very hard tablets tend to 'cap' or lose their crown portions on attrition. Such tablets tend to powder, chip and fragment. 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.

4.2 Official tests:

They are found and registered into pharmacopeia and give the final decision about accepting or rejecting the batch of tablets

1. Content of Active Ingredient
2. Uniformity of Weight/ Weight variation test
3. Content uniformity test
4. Disintegration test
5. Dissolution

4.2.1 Content of Active Ingredient

This is determined from a sample of 20 tablets which should be randomly selected from a batch of tablets. The tablets are weighed together and are crushed in a mortar with a pestle.

An amount equivalent to the theoretical content of each tablet or the average of the crushed tablets is weighed out in an analytical balance. The weighed powder is dispersed in a solvent in which the active drug is freely soluble or in a solvent prescribed in the individual drug monograph.

This is filtered and an aliquot of the resultant filtrate is subjected to the stipulated assay procedures. The assay procedures are usually given in the individual drug monograph.

Analysis of the active drug is usually carried out using spectrophotometry or High-Performance Liquid Chromatography (HPLC). The formulation scientist must be familiar with Beer-Lambert's law. This could be found in relevant analytical textbooks.

It must be emphasized that the results obtained here gives the average content of 20 tablets but does not give indication of the variation of drug content among the individual tablets. The limits of acceptance or rejection of tablets batches are usually presented in the individual drug monograph.

4.2.2 Uniformity of Weight/ Weight variation test

Several investigators have assessed the weight-variability issues associated with tablet splitting as measured by mean weight, standard deviation (SD), and coefficient of percent of variability; weight uniformity, as measured by percent of CV% or weight, as measured by mean ± SD. 8,21-29 In addition, stability issues associated

with tablet splitting have been evaluated in studies by Margiocco and Volpe and colleagues. [5]

The test for uniformity of weight is performed by weighing individually 20 tablets randomly selected from a tablet batch and determining their individual weights. The individual weights are compared with the average weight.

The sample complies with USP standard if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.

Coated tablets are exempted from these requirements but must conform to the test for content uniformity. [7]

Acceptance Criteria

Average mass of tablets	***Average mass of tablets***
<80 mg	±10.0
80-250 mg	±7.5
>250 mg	±5.0

1. If 1 tablet is out of the range, but less than double the allowed %(pass)
2. If 2 tablets are out of the range but less than double the allowed % (pass)
3. If 3 tablets deviated more than the allowed range % (failed).
4. If only one deviate more than the double allowed limit (failed).

4.2.3 Content uniformity test

It was developed to ensure content consistency of active drug substances within a narrow range around the label claim in dosage units. This test is crucial for tablets having a drug content of less than 2 mg or when the active ingredient comprises less than 2% of the total tablet weight.

By the USP method, 30 tablets are randomly selected, 10 of these tablets are assayed individually according to the method described in the individual monograph. Unless otherwise stated in the monograph, the requirements for content uniformity are met if the amount of active ingredient in nine (9) of the ten (10) tablets lies within the range of 85% to 115% of the label claim. The tenth tablet may not contain less than 75% or more than 125% of the labelled drug content.

If one or more dosage units do not meet these criteria, the remaining 20 tablets are assayed individually and none may fall outside of the 85% to 115% range for the batch to be accepted.

Various factors are responsible for the variable content uniformity in tablets. This may include the tablet weight variation because uneven distribution of the drug in the powder or granules due to the segregation of the powder mixture or granulation during formulation processes [7].

4.2.4 Disintegration test:

For the medicinal agent in a tablet to become fully available for absorption, the tablet must first disintegrate and discharge the drug to the body fluids for dissolution.[1] Disintegration tests are, however, useful for assessing the potential importance of formulation and process variables on the biopharmaceutical properties of the tablet, and as a control procedure to evaluate the quality reproducibility of the tablet during production. Research has established that one should not automatically expect a correlation between disintegration and dissolution, since the dissolution of a drug from the fragmented tablet control the appearance of the drug in the blood. Disintegration is a (guide for an optimum tablet formula) and (as an in-process control test to ensure lot-to-lot uniformity) [3]. A disintegration instrument consists normally of six chambers, i.e. tubes open at the upper end and closed by a screen at the lower. Before disintegration testing, one tablet is placed in each tube and normally a plastic

disc is placed over the tablet. The tubes are placed in a water bath and raised and lowered at constant frequency in the water in such a way that at the highest position of the tubes, the screen (and thus the tablet held down by the plastic disc) remains below the surface of the water.

The test is carried out by agitating a given number of tablets in an aqueous medium at a defined temperature 37C and the time to reach the endpoint of the test is recorded. The preparation complies with the test if the time to reach this endpoint is below a given limit. The endpoint of the test is the point at which all visible parts of the tablets have been eliminated from a set of tubes in which the tablets have been held during agitation. The tubes are closed at the lower end by a screen and the tablet fragments formed during the disintegration are eliminated from the tubes by passing the screen openings, i.e. disintegration is considered to be achieved when no tablet fragments remain on the screen (fragments of coating may however remain).[2]

The procedures are stated for running disintegration time for uncoated tablets, plain-coated tab., enteric coated tab., buccal tab., and sublingual tab.). Uncoated USP tablets (disintegration time 5 min (aspirin tablets), but majority of the tablets have a maximum disintegration time of 30 min. Enteric coated tablets are not to disintegrate after 1 hr in simulated gastric fluid. The same tablets are then tested in simulated intestinal fluid and are to disintegrate in 2 hrs plus the time specified in the monograph [3].

4.2.5 dissolution of tablet

Dissolution testing is the most important way to study, under in vitro conditions, the release of a drug from a solid dosage form and thus represents an important tool to assess factors that affect the bio- availability of a drug from a solid preparation. During a dissolution test, the cumulative amount of drug that passes into solution is

measured as a function of time. The test thus describes the overall rate of all the processes involved in the release of the drug into a bioavailable form.

The selection of medium and volume is guided by the aim of the dissolution test, solubility of the drug and type of apparatus used. All tests are con- ducted at 37 °C to mimic body temperature [2].

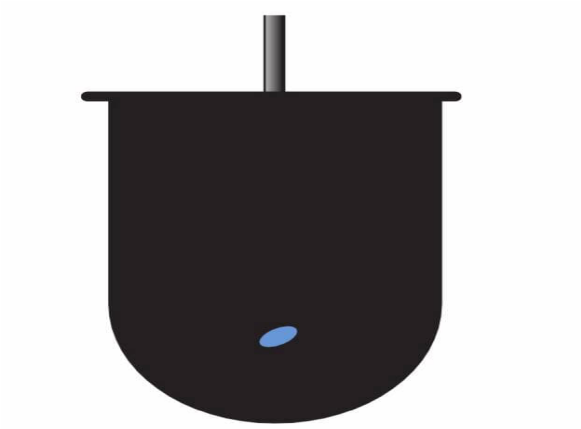
There are currently four dissolution apparatus described in the US and European Pharmacopoeias for the testing of oral solid drug products. These are the basket and paddle apparatus, the reciprocating cylinder and the flow through cell The selection of dissolution apparatus depends mainly on the solubility of the drug and type of dosage form [2].

The first-choice equipment for QC dissolution testing are the basket and paddle apparatuses because their simple design makes them ideal for routine use. However, due to the limited volume of medium and operational difficulties in medium change, these apparatuses are often more suited to immediate-release than the modified release products, and in particular immediate-release formulations of soluble drugs.

The reciprocating cylinder and flow through cell system are particularly useful for testing of modified-release (MR) dosage forms and poorly soluble drugs, respectively. A brief description of each apparatus is given below.

4.2.5.1 Basket apparatus (USP Apparatus 1)

The basket apparatus was the first of official dissolution tester to be described in the USP in 1970 and remains one of the most commonly used methods for testing the dissolution of capsules and tablets [2].



• Basket apparatus (USP Apparatus 1).

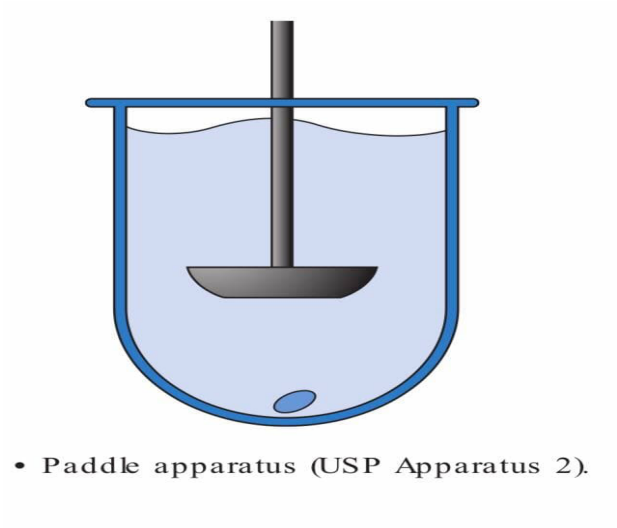
Basic components of the apparatus are a perforated stationary sample basket, a rotating filter-stirrer assembly, and a closed jacketed dissolution fluid container.[8]

In this apparatus, the dosage form is placed inside a rotating basket made of a stainless steel wire mesh and immersed in dissolution medium which has been pre-warmed at 37°C.

During the test, the basket rotates at a constant speed, typically set between 50 and 100 rpm. The dissolution medium is contained in a glass cylindrical vessel with a spher- ical bottom and with a nominal capacity of no less than 1 L. The dissolution medium volume used with this method is normally 0.9 L, although lower (0.5 L) and higher (4 L) volumes may also be employed. The composition and/or pH of the medium may be changed by manually replacing it or by adding media of different composition. At pre- determined times, samples of dissolution medium are removed and analyzed for drug content [2].

4.2.5.2 Paddle apparatus (USP Apparatus 2)

Following its introduction in the USP in 1978, the paddle apparatus became the most widely used dis- solution tester. It utilizes the same dissolution vessels as the basket apparatus but here the dosage form is positioned at the centre bottom of the vessel [2].



• Paddle apparatus (USP Apparatus 2).

The paddle apparatus (Apparatus II) consists of a special, coated paddle that minimizes turbulence due to stirring. The paddle is attached vertically to a variable-speed motor that rotates at a controlled40 speed. The tablet or capsule is placed into the round-bottom dissolution flask, which minimizes turbulence of the dissolution medium. The apparatus is housed in a constant-temperature water hall maintained at 370C, similar to the rotating-basket method. The position and alignment of the paddle are specified in the USP. The paddle method is very sensitive to tilting. Improper alignment may drastically affect the dissolution results with some drug products [9].

5 Conclusion

Quality control of tablets involves various tests which require keen attention. To ensure that established product quality standards are met, these tests must be performed during production (in-process controls) and verified after the production of each batch.

6 References

1- Loyd V. Allen, Jr. Howard C. Ansel. **Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems.** Allen, Loyd V., Jr. **Tablet**. Philadelphia. 2001. 263-298

2- Kevin M. G. Taylor,Michael E. Aulton . **Aulton 's Pharmaceutics**. Göran Alderborn. **Tablets and compaction** .1988. 504-550

3- Leon Lachman, Herbert A. Lieberman, Joseph L. Kanig. **The Theory and Practice of Industrial Pharmacy**. GILBERT S. BANKER and NEIL R. ANDERSON . **Tablet** . Philadelphia . 1986 . 293_345

4- Mohammad Saleem, Mohammad Shahin, Bijja Srinivas ,Ashraf Begum. **Evaluation of tablet by friability apparatus**. IJRPC. 2014: 4(4); 837-840.

5- Freeman, M. K., White, W., & Iranikhah, M. **Tablet Splitting: A Review of Weight and Content Uniformity.** The consultant pharmacist. 2012, 27(5). 341-352

6- Pharma approach. **Quality control tests for tablet**. 2021, https://www.pharmapproach.com/quality-control-tests-for-tablets/2/

7- Hiestand, E. N., Well, J. E., Pool, C. B., Ocks, J. F.: **Physical processes of tableting.** J. Phaim. Sci. 1977, 66:510-519.

8- Ashok C Shah, Craig B Peot, John F Ochs. **Design and evaluation of a rotating filter-stationary basket in vitro dissolution test apparatus I: Fixed fluid volume system.** Journal of pharmaceutical sciences, 1973, 62 (4), 671-677.

9- Mitul Shah. **Drug Dissolution Apparatus II USP (Paddle)**. pharma tip. Views: 42745 | Date: 24-Mar-2011.