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Study of Quality Control Tests for Different Types of Paracetamol Tablets in Iraqi Markets and Their Effects on Health and the Environment: A Review

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ABSTRACT

Quality management, quality control, and quality assurance are three interrelated concepts that are essential for ensuring the quality of products and services. Quality management is the overall approach that an organization takes to managing and improving the quality of its products or services. It encompasses both quality control and quality assurance, as well as other activities such as training employees, engaging with customers, and setting quality goals and objectives. 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.

KEYWORDS: *quality management, quality control, quality assurance, pharmacopoeia, world health organization, tablet*

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INTRODUCTION

Quality management

Quality management is the overall approach that an organization takes to managing and improving the quality of its products or services. It encompasses all aspects of the organization's activities, from product design and development to production, sales, and customer service. The goal of quality management is to ensure that the organization's products and services meet the needs and expectations of its customers. This is achieved by establishing and implementing quality standards, processes, and systems. Quality management also involves continuous improvement, which means that the organization is constantly looking for ways to improve its products, services, and processes [1,2,3].

Quality control

Quality control is the part of quality management that focuses on fulfilling quality requirements. he 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 [3,4]. 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 preformation and physical, chemical,

therapeutic, and toxicologic 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 [5].

Quality assurance

Quality assurance is the part of quality management that focuses on preventing defects and ensuring that the quality management system is effective and consistent. It involves activities such as process improvement, training, and auditing[6,7]. Quality assurance activities are designed to identify and eliminate potential problems before they occur. This helps to ensure that products and services a 1 produced to a high standard and that they meet th.. needs and expectations of customers. g. The assurance of product quality depends on more than just proper sampling and adequate testing of various components and the finished dosage form[8]. 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 [9,10].

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 [11,12].

Pharmaceutical solid dosage form

Pharmaceutical solid dosage forms for oral use are the most common pharmaceutical formulation types worldwide. They are complex multicomponent system that may be available in many diverse structures such as powders, granule, compressed tablet, chewable tablet and capsules as represented in Figure 1.1. Solid oral dosage forms were the first dosage forms to be considered for worldwide regulation by the International Conference on Harmonization (ICH)[13,14,16]. The ICH is a collaborative effort by both industry and regulatory bodies of the United States, the European Union, and Japan. Preliminary physicochemical assessment of drug products has a paramount importance in ensuring the quality of drug products. Generic drug products must satisfy the same standards of quality, efficacy and safety as those applicable to the innovator products. The problem of quality assessment of pharmaceutical solid dosage form is important all over the world [17,18,19]. Ensuring the quality of medicine is becoming more important and challenging. This generates the need for more fast and smart technique to fulfil the requirement. Different techniques are utilized for the analysis of the solid oral dosage form. The one which is used in the modern times are including; Microscopy, X ray Powder Diffractions, Thermal Analysis, Fourier Transform Infrared (FTIR), Micro spectroscopy, Nuclear Magnetic Resonance (NMR) Imaging, Near Infrared (NIR) Analysis, and Raman Spectroscopy [20,21,22]

Figure 1.1. Pharmaceutical solid dosage forms

Tablets

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 as shown in Figure 1.2. Most tablets are used in the oral administration of drugs[23,24]. 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.

Figure.1.2. Tablet dosage forms

Advantage of tablet

1. The oral route represents a convenient and safe way of drug administration.**2**. The preparation procedure enables accurate dosing of the drug **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.**4.** Their cost is lowest of all oral dosage forms.**5.** They are in general the easiest and cheapest to package and ship of all oral dosage forms.**6.** 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.**7.** They are better suited to large-scale production than other unit oral forms [25, 26].

Disadvantages of tablet

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.** Some drugs may cause local irritant effects or otherwise cause harm to the gastrointestinal mucosa **3.** Some drugs resist compression into dense compacts, owing to their amorphous nature or flocculent, low-density character. **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 [27,28].

Evaluations

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 [29,30]. 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 as given in Figure 1.3. and these tests are traditionally concerned with the content and the in vitro release of the active ingredient. e methods of tablet assessment generally classified into non-official (or nonpharmacopeial) tests and official (or pharmacopeial) tests[31].

Figure 1.3. List of pharmacopeia

Paracetamol

Paracetamol (acetaminophen) belongs to the NSAIDs family. It is widely used and well known by Iraqi population for headache relief and its antipyretic effects. Paracetamol is available as over the counter drug (OTC) and it is available in different dosage forms and different strengths [32].

Medical uses of paracetamol

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 antiinflammatory effects. Generally, paracetamol can be used to treat several conditions such as headache, muscle ache, fever and cold, arthritis, backache, toothache. Paracetamol combined with opioid pain is also used for severe pain such as cancer pain and pain after surgery [33].

Pharmacokinetics of paracetamol

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 [34].

Side effects of paracetamol

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 [35].

Dose and dosage forms of paracetamol

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[36]. The recommended doses of paracetamol in different age groups are listed in Table 1.1.

Table 1.1 The recommended doses of paracetamol based on age of patients.

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

Mechanism of Action of Paracetamol

Paracetamol (acetaminophen) is generally considered to be a weak inhibitor of the synthesis of prostaglandins (PGs). However, the in vivo effects of paracetamol are similar to those of the selective cyclooxygenase-2 (COX-2) inhibitors. Paracetamol also decreases PG concentrations in vivo, but, unlike the selective COX-2 inhibitors, paracetamol does not suppress the inflammation of rheumatoid arthritis as represented in Figure 1.4.[37].

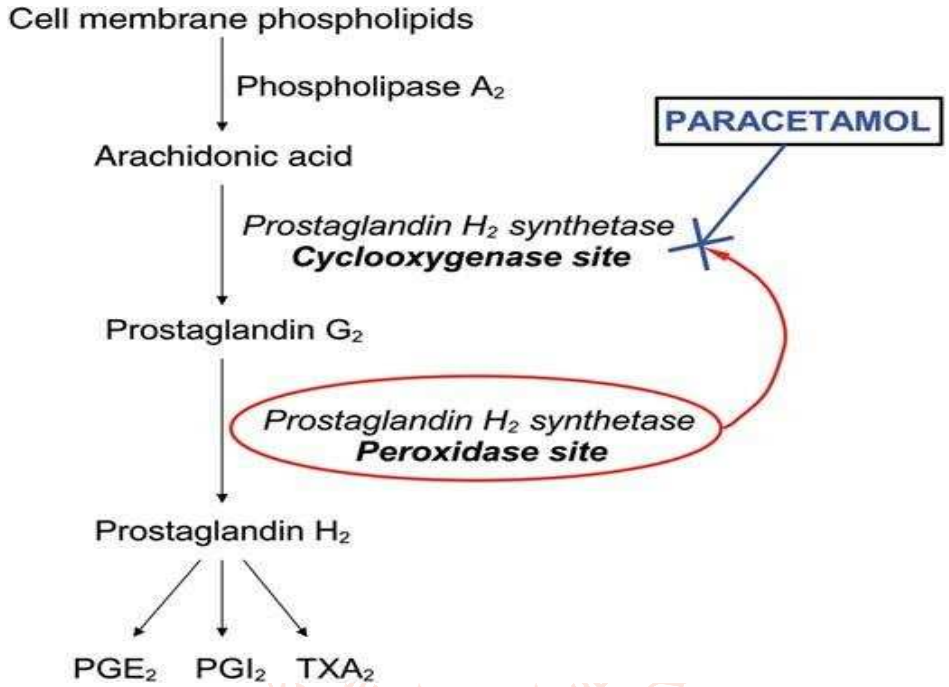

Figure 1.4. Role of paracetamol in inhibition of prostaglandin production

In this project we subjected five types of paracetamol tablets from different companies which are widely used in the private pharmacies in Hilla city to quality control tests to indicate whether these products will fit to the standard criteria of the United States Pharmacopeia or not. The types chosen were based on price criteria (cheap, moderate and relatively expensive) and based on the manufacturer (local private and government factories and international factories including Indian and European manufacturer).

MATERIALS AND METHODS

Materials

Paracetamol sheets from five different companies were bought from a native pharmacy in Hilla city. The selected types included Safacetol (SAFA Co.), Omol (NP Pharma Co.), Paracetol (SDI Co.), Apmol (AJINTA Co.) and Supofen (BASI Co.) which are shown in Figure 2.1.

Figure2.1. Different types of paracetamol used in project.

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), Figure 2.2. The process was repeatedly performed for each type of paracetamol from different companies.

Figure 2.2 Physical examination of different types of paracetamol tablets.

Weight variation test

Ten tablets where removed from the sheet and the weight of each tablet was measured individually by H-digital sensitive balance (DENVER Instrument /China), Figure 2.3. The mean and standard deviation were calculated and the accepted values of variation of ±5% were measured and compared with the standard deviation [38].

Figure2.3. Four digits sensitive balance used for weight variation of different types ofparacetamol tablets.

Size variation test

Ten tablets were removed from the sheet and each tablet was placed in digital caliper (WEILIANG Co./ China), Figure2.4 to measure its height. The steps were repeated the rest of the tablets and then mean and standard deviation were calculated and compared with the accepted ±5% value [39].

Figure 2.4. digital scale used for size variation of different types of paracetamol tablets.

Friability test

Friability is the tendency of tablet to powder, chip or fragment and this can affectthe 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), Figure 2.5to measure friability of the different brand of paracetamol tablet.

Figure 2.5. Friability tester used for used for different types of paracetamol tablets

The weight of 10 tablets of each brand of paracetamol where measured and the tablets were loaded in the friability tester. The apparatus exposed tablets to rollingand repeated shocks as they fall 6 inches in each turn within apparatus. After 4 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:

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

Where $W_{initial}$ is the initial weight and W_f is final weight

Friability values more than 5**%** were considered as unacceptable based on the USP [40].

Disintegration test

Disintegration is a process by which tablets are fragmented into granules or smallparticles. It is defined as the time required for a group of tablets to fragment into particles under a given set of conditions which is measured by disintegration tester. This test is basic for tablets intended that administration by mouth except those intended to be chewed before being swallowed or those that should dissolve slowly in the mouth, e.g. lozenges, glyceryl trinitrate, or effervescent tablets. Also, disintegration does not apply to similar types of sustained-release tablets. Before each step the apparatus (Disintegration tester \GUOMING CS-2 / China) Figure 2.6. was cleaned from any residue of another test. The tank of the device was filled with distilled water and left to reach the desired temperature (37ºC). Six tablets of paracetamol were used by putting one tablet in each basket of the 6 tubesand fixed by the specified disk. The device was operated to start continuous immersing and lifting of the tubes in the tank. The tablets in each tube were carefully monitored until disintegrated completely and the time was recorded. Themean and standard deviation of the disintegration time were calculated and compared between different paracetamol brands. Values less than 10 minutes (600seconds) were considered as accepted values [41].

Figure 2.6. Disintegrator apparatus used for different types of paracetamol tablets

Hardness test

Hardness test (crushing strength) is the load required to crushing the tablet whenplaced on its edge. Hardness is the force required to break the tablet by diametriccompression 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), Figure 2.7 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/cm^2 [4]. Values outside this range were considered unaccepted results[42].

Figure 2.7 Manual tablet hardness tester used for different types of paracetamoltablets

RESULTS AND DISCUSSIONS

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 [5]. 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 protectsthe 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 establishedproduct quality standards are met.

Physical examination

The various types of paracetamol tablets were subjected to physical examinationusing naked eye. The shape, engravings, color, sharpness of edges and extent of powder loss were investigated and the results are listed in Table 3.1.

Table 3.1 Physical examination of different paracetamol brands.

Product	Description
Paracetol	Round, white tablets with excessive loss of powders and irregular edges. The tablets contain break-line with engraved with "500" sign.
Safacetol	Round, white tablets with loss of powders and irregular edges. The tablets contain a break-line with no engravings.
Sapofen	Round, white tablets with moderate loss of powders and irregular edges also. The tablets do not contain break-line nor any engravings.
Apmol	Round, white tablets with excessive loss of powders and regular edges.
Omol	Round, white tablets with excessive powder loss and few tablets with irregular edges. The tablets contain a break-line with no engravings.

Weight variation

The average weights of ten paracetamol tablets of each brand were measured as well as the standard deviation and the accepted values based on the ± 5%. The results are listed in Table 3.2.

Table 3.2 Weight variation of different paracetamol brands

Product	Weight (mg)	SD	Acceptable value	Verdict
Paracetol SDI	616.07	9.19	30.80	Approved
Safacetol	605.73	6.31	30.28	Approved
Sapofen	681.64	10.72	34.08	Approved
Apmol	581.41	51.98	29.07	Rejected
Omol	555.93	7.11	27.79	Approved

The lowest weight variation was detected in Omol brand. The data indicated thatall types of paracetamol tablets were within the accepted range except the Apmoltype. The variation in weight in tablets dosage form may be caused by several factors such as flow properties of powders, size and shape of particles and the amount and type of excipients.

Size variation

The average size of ten paracetamol tablets of each brand were calculated as well as the standard deviation and the accepted values based on the ± 5%. The results areshown in Table 3.3.

Table 3.3. Size variation of different paracetamol brands

Product	Size (mm)	SD	Acceptable value	Verdict
Paracetol SDI	4.303	0.095	0.215	Approved
Safacetol	4.369	0.286	0.218	Rejected
Sapofen	4.273	0.255	0.233	Rejected
Apmol	4.273	0.096	0.213	Approved
Omol	4.137	0.124	0.206	Approved

Two types of paracetamol (Safacetol and Sapofen) failed to pass the test of size variation while the rest of the types were within the accepted range. The ParacetolSDI and Apmol brands showed the best values with minimum size variation.

The thickness of a tablet is determined by the diameter of the die, the amount of fill permitted to enter the die, the compaction characteristics of the fill material, and the force or pressure applied during compression. Many of these factors are affected by the flow properties of powders, size and shape of particles and the amount and type of excipients (glidants). To produce tablets of uniform thicknessduring and between batch productions for the same formulation, care must be exercised to employ the same factors of fill, die, and pressure.

Friability test

Friability is the phenomenon where the surface of the tablet is damage or shown a site of damage due to mechanical shock. The purpose of the test is to evaluate the ability of the tablets to withstand the breakage during the packaging,transportation and handling. The average percentages of weight loss of paracetamol tablets of each brand were calculated and the accepted values based on the ± 5%.The results are shown in Table 3.4.

Table 3.4 percentage of weight loss of different paracetamol brands

Product	% Wt. loss	Verdict
Paracetol SDI	7.71	Rejected
Safacetol	6.53	Rejected
Sapofen	7.29	Rejected
Apmol	0.2	Approved
Omol	0.24	Approved

The results revealed that only 2 brands of paracetamol (Apmol and Omol)succeeded to pass the test. However, other brands (Paracetol SDI, Safacetol and Sapofen) were out of the accepted range. The friability is affected by the type andamount of binder, method of preparation and the force of compression.

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 fordissolution. Tablet disintegration also is important for tablets containing medicinal agents (such as antacids and antidiarrheals) that are not intended to be absorbed but rather to act locally within the gastrointestinal tract. In these instances, tabletdisintegration provides drug particles with an increased surface area for activity within the gastrointestinal tract. All USP tablets must pass a test for disintegration,which is conducted *in vitro* using a disintegrator testing apparatus. The average disintegration time of different paracetamol brands were determined and the results are shown in Table 3.5.

Table 3.5. Disintegration time of different paracetamol brands.

Product	Disintegration time ± SD (sec)	Verdict
Paracetol SDI	109 ± 11	Approved
Safacetol	378 ± 68	Approved
Sapofen	161 ± 21	Approved
Apmol	34 ± 5	Approved
Omol	141 ± 21	Approved

The disintegration of all types of paracetamol tablets were accepted and below theten minutes threshold. However, the fastest time was shown by Apmol brand (34 sec). The faster disintegration time will improve rate of dissolution rate of absorption, bioavailability, rapid onset of action and faster response [6]. The longest disintegration time was related to Safacetol brand which reached almost 7minutes.

Hardness test

Generally, the greater the pressure applied, the harder the tablets, although the characteristics of the granulation also have a bearing on hardness. Certain tablets,such as lozenges and buccal tablets, are intended to dissolve slowly and are intentionally made hard; other tablets, such as those for immediate drug release, are made soft [6]. In general, tablets should be sufficiently hard to resist breaking during normal handling and yet soft enough to disintegrate properly after swallowing. A force of about 4 kg is considered the minimum requirement for a satisfactory tablet. Multifunctional automated equipment can determine weight, hardness, thickness, and diameter of the tablet. The average hardness of differentparacetamol brands were determined and the results are shown in Table 3.6. It should be kept in mind that this test was performed using a manual device which gives rough results rather the automatic apparatus, thus results close to 10 kg/cm^2 were considered as approved results.

Table 3.6 Hardness of different paracetamol brands.

Product	Hraness ± SD (Kg/cm^2)	Verdict
Paracetol SDI	12.21 ± 1.3	Approved
Safacetol	12.23 ± 1.1	Approved
Sapofen	11.01 ± 1.4	Approved
Apmol	10.32 ± 0.9	Approved
Omol	9.31 ± 1.1	Approved

CONCLUSION AND RECOMMENDATION

The data indicated that all brands succeeded to pass most quality control tests with some exceptions. It should be highlighted these results were obtained for the specific batches used in the experiment, however, different results may be obtained if different batches were used for the same products and this is the core of quality control studies. One of the major tests of quality control for tablets is the quantitative determination of the tablets contents especially for the active ingredient(s). Unfortunately, this test was not performed in our project due time and facility limitations. However, such test (quantitative determination of paracetamol contents in each brand using high performance liquid chromatography) could be included in any future work to shed more light on this issue and strengthen the scientific aspects of the project.

REFERENCES

[1] Standardization, I. O. f. (2005). Quality Management Systems--Fundamentals and Vocabulary, International Organization for Standardization.

[2] Natiq, M. "Define & Differentiate Between Quality Management, Quality Control, and Quality Assurance: A Review of Physical and Chemical Quality Control Tests for Solid Dosage Forms, Liquids, and Parenteral."

[3] Ndihokubwayo, J.-B., et al., Implementation of the World Health Organization Regional Office for Africa stepwise laboratory quality improvement process towards accreditation. African journal of laboratory medicine, 2016. 5(1): p. 1-8

[4] Lachman, L., et al. (1976). The theory and practice of industrial pharmacy, Lea & Febiger Philadelphia.

[5] Shargel, L., et al. (1999). Applied biopharmaceutics & pharmacokinetics, Appleton & Lange Stamford.

[6] Aulton, M.E., Pharmaceutics: The science of dosage form design. (No Title), 2002.

[7] Swarbrick, J., Encyclopedia of Pharmaceutical Technology, pdf.

[8] Mahato, R. I. and A. S. Narang, Pharmaceutical Dosage Forms and Drug Delivery: Revised and Expanded. 2017: CRC Press.

[9] Al-Achi, A. and P. Kulkarni, Rheological Measurements of Compounded Emulsion s and Suspensions: A Laboratory Exercise to Support Theoretical Learning. J Pharm Pract Pharm Sci, 2019. 1: p. 28-32.

[10] Bhurat, M.R., et al., Evaluation of Eulophia herbacea tubers mucilage as an innovative suspending agent. J Pharm Res, 2012. 5(1): p. 321-323.

[11] Yacuzzi, E.A., et al., The sources of quality in the pharmaceutical industry. 2004, Serie Documentos de Trabaj.

[12] Lexchin, J., et al., Pharmaceutical industry sponsorship and research outcome and quality: systematic review. bmj, 2003. 326(7400): p. 1167-1170.

[13] Rohit S Gupta, Ratnadeep R Deshmukh, Priyanka U Randive, Akshay V Kshirsagar, Jaypalsing N Kayte (2018) Study of Pharmaceutical Solid dosage forms using Invasive and Non Invasive Techniques.

[14] Krylov SN, Dovichi NJ (2000) Capillary electrophoresis for the analysis of biopolymers. Anal Chem 72: 111R-128R.

[15] Ren JC (2000) High-throughput single-strand conformation polymorphism analysis by capillary electrophoresis. J. Chromatogr. B 741: 115-128. 4. Oda RP, Landers JP (1997) Introduction to capillary electrophoresis. In Handbook of Capillary Electrophoresis. In: Landers (Eds.), (2nd edn), CRC Press, NewYork, USA, p. 1-47.

[16] Itiola OA, Pilpel N (1996): effects of interaction on the disintegration and dissolution of metronidazole tablets.pharmazie 51: 987-989.

[17] USP (1999) 24 US Pharmacopeia Convention, Rockville, MD, pp. 299-301.

[18] Jose Manuel Amigo (2010) Practical issues of hyperspectral imaging analysis of solid dosage forms, Anal Bional Chem pp. 93-109-114.

[19] Salvador Garrigues (2013) Miguel de la Guardia, "Non-invasive analysis of solid samples", Trends in Analytical Chemistry 43: 161-173.

[20] Skoog DA, West DM, Holler FJ (1996) Fundamentals of Analytical Chemistry, (7th edn), Saunders College Publishing, Philadelphia.

[21] Jones AJ, Martin AJP (1952) Gas-liquid partition chromatography: a technique for the analysis of volatile materials. Analyst 77: 915-918.

[22] Snyder LR, Kirkland JJ (1982) Introduction to High Performance Liquid Chromatography, (2nd edn), Chapman and Hall, London, UK.

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

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

[25] 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.

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

[27] 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/

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

[29] Prakash J, Srivastava S, Ray RS, Singh N, Rajpali R, Singh GN. Current status of herbal drug standards in the Indian pharmacopoeia. Phytotherapy Research, 2017 Dec; 31(12): 1817-23.

[30] Pharmacopoeia I. Ghaziabad: Indian Pharmacopoeial Commission. Govt. of IndiaMinistry of Health and Family W 2014; 1948.

[31] Pharmacopoeia BH. The British Pharmac Commission Secretariat of the Medicines and Healthcare Products Regulatory Agency (MHRA). Publisher: TSO (The Stationery Office), 2019.

[32] Sheen CL, Dillon JF, Bateman DN, Simpson KJ, Macdonald TM (2002) Paracetamol toxicity: epidemiology, prevention and costs to the health-care system. QJM 95: 609-619.

[33] Prescott K, Stratton R, Freyer A, Hall I, Le Jeune I (2009) Detailed analyses of self-poisoning episodes presenting to a large regional teaching hospital in the UK. Br J Clin Pharmacol 68: 260-268.

[34] Bergen H, Hawton K, Waters K, Cooper J, Kapur N (2010) Epidemiology and trends in non-fatal self-harm in three centres in England: 2000-2007. Br J Psychiatry 197: 493-498.

[35] Larson AM, Polson J, Fontana RJ, Davern TJ, Lalani E, et al. (2005) Acetaminophen-induced acute liver failure: results of a United States multicenter, prospective study. Hepatology 42: 1364-1372.

[36] Nourjah P, Ahmad SR, Karwoski C, Willy M (2006) Estimates of acetaminophen (Paracetomal)-associated overdoses in the United States. Pharmacoepidemiol Drug Saf 15: 398-405.

[37] Chun LJ, Tong MJ, Busuttil RW, Hiatt JR (2009) Acetaminophen hepatotoxicity and acute liver failure. J Clin Gastroenterol 43: 342-349.

[38] Society of Japanese Pharmacopoeia. Japanese Pharmacopoeia, 16th Edition, Pharmaceuticals and Medical Devices Agency, Japan, 2011.

[39] World Health Organization (WHO). International Pharmacopoeia, 5th Edition, WHO, Switzerland, 2015.

[40] E Jatto, AO Okhamafe. An overview of pharmaceutical validation and process controls in drug development. Trop J Pharm Res. 2002;1(2):116-117.

[41] LV Allen, NG Popovich, HC Ansel. Ansel's pharmaceutical dosage forms and drug delivery systems. 9th ed. New York: Lippincott Williams & Wilkins; 2011.

[42] E Jatto, AO Okhamafe. An overview of pharmaceutical validation and process controls in drug development. Trop J Pharm Res. 2002;1(2):116-117.

[43] Supplementary guidelines on good manufacturing practices: validation, Appendix 4 on Analytical method validation, in WHO Technical Report Series, No. 937, 2006, Annex 4, and ICH guideline Q2 (R1).

[44] Fuhrman, L., Jr. (2006). Ansel's pharmaceutical dosage forms and drug delivery systems, 8th edition. American Journal of Pharmaceutical Education, 70(3), 71.