Evaluation of the quality control parameters of different brands of paracetamol available in Bangladesh Pharma market

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

Submitted by: Fahmida Zaman Shimul

ID: 2008-3-70-040

Department of Pharmacy

East West University

10 July, 2012

Acknowledgements

All praise to the Almighty, who has made all things in my life possible. It is Him who has sustained me throughout the course of my study.

I would like to extend my sincere thanks to the East West University for giving me the opportunity and for seeing sufficient merit in me to allow me to conduct doing in the EWU laboratory of the Department of Pharmacy. I am greatly indebted to my supervisor Apurba Sarker Apu, Senior Lecturer, EWU, for his scholarly guidance from the germinal to the terminal end of this work.

I wish to extend my sincere gratitude to my co supervisor Dr. Sufia Islam, Chairperson and Associate Professor, EWU, for facilitating learning through sharing of knowledge at EWU as well as for his kind guidance. Special thanks go to all the academic staff of the Department for their inspiration during the course. I also acknowledge the assistance of Sujit Kumar, Lab Instructor for the Advanced Analysis Laboratory of EWU who painstakingly supervised all my instrument handling in the laboratory.

Special thanks to Arindom Pal, Lecturer, EWU, for helping on the survey of Bangladesh Paracetamol Pharma market. I would also like to thank my research co-workers Zinia Mosharraf whose assistance during the lab work aided in the process of easing my workload.

Last but not least, I want to thank my father Md. Ashrafuzzaman, my mother Sakia Begum and my uncle Golam Robbany for all that they have been to me and their relentless support. I sincerely value their love, sacrifices, encouragement, inspiration and unconditional mental support. I am also grateful to my friends for encouraging me to accomplish this study.

Fahmida Zaman Shimul

Certificate

Declaration by the Research Supervisor and Department Chairperson

July 2012

It is pleasure to certify that the research paper titled 'Evaluation of Quality control parameters of different brand of Paracetamol available in Bangladesh pharma market' is prepared by Fahmida Zaman Shimul, a student of the Department of Pharmacy, East West University, Dhaka. She prepared the paper under our supervision. This is her original work.

Dr. Sufia Islam

Chairperson & Associate Professor

Department of Pharmacy

East West University

Apurba Sarker Apu

Senior Lecturer

Department of Pharmacy

East West University

Dedication

This Paper Is Dedicated To

My Uncle Gulam Rabbani

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Abstract

Purpose: The research work was carried out to evaluate the quality control parameters of 15 different batches of 5 different brands of Paracetamol tablets available in Bangladesh pharma market by means of weight variation test, friability test, hardness test and disintegration test.

Method: Forty six tablets of each batch of 5 different brands were collected from market and the physical parameters of these five brands were evaluated by means of weight variation, hardness, friability and disintegration test. The variation of the weight of individual tablet is a valid indication of the corresponding variation in the drug content and scheming tablet weights within the BP or USP limit contribute to better tablet hardness and friability. Hardness is the second most important physical facet for assessing tablet which indicates the capability of a tablet to withstand mechanical shocks during handling in manufacturing, packaging and shipping. Friability test is essential to evaluate the ability of a tablet to withstand abrasion in packing, handling and transporting as well as disintegration test is crucial physical feature which is considered as the first step toward dissolution.

Result: The weight variation of three different batches of ACE tablet (1100304, 1100274 and 1110202), FAST tablet (XC1099, XC1021 and XC1076) and XCEL tablets (LE31, KE125 and OE136) comply with the specification mentioned in the USP and pass the quality control parameter. The weight variation of two different batches of XPA tablet did not comply with the USP specification. Batch 11L33 comply with the USP specification but batch 11128 and batch 12A03 did not comply with the USP specification. The weight variation of three different batches of SERVIGESIC tablet (2017, 1998 and 8914) complies with the specification mentioned in the USP and passes the quality control parameter. All three batches of ACE (1100304, 1100274 and 1110202), FAST (XC1099, XC1021 and XC1076), XCEL (LE31, KE125 and OE136), XPA (11L33, 11128 and 12A03) and SERVIGESIC (1998, 8914 and 2017) have a hardness greater than 4kg and, therefore, meet the USP

specification and pass the quality control parameter. All three batches of ACE (1100304, 1100274 and 1110203), FAST (XC1099, XC1021), XCEL (LE31, KE125 and OE136), XPA (11L33, 11128 and 12A03) and SERVIGESIC (1998, 8914 and 2017) have met the USP specification and passed the friability test. However XC1076 batch of FAST brand does not meet the USP specification. On the other hand all three batches of ACE tablets (1100304, 1100274, 1110202), FAST (XC1099, XC1021 and XC1076), XCEL (LE31, KE125 and OE136), XPA (11L33, 11128 and 12A03) and SERVIGESIC (1998, 8914 and 2017) have met the USP specification and passed the disintegration test.

Conclusion: Quality control parameters or physical properties of tablet are useful tools for better quality of medicines and for maintaining consistency in batch-to-batch manufacturing and it should be performed for every drug product. From this study it was observed that except two batch of XPA and one batch of FAST all the different brands of paracetamol meet the quality control parameter specifications. This study revealed that all the quality control parameters are closely related to each other and since all the quality control tests did not conducted in this study, further studies are needed to assess the quality of the products.

Keywords: hardness, friability, disintegration, weight variation, BP, USP.

Chapter -1
Introduction

1.1 Introduction

1.2 Overview:

Evaluation of the quality control parameters of different brands of paracetamol available in Bangladesh Pharma market involves all activities undertaken to obtain more data and information about the Paracetamol after it has been granted marketing authorization and made available for public use. The obtained quantitative and qualitative data can be employed in the development and improvement of the product. This post−marketing quality control parameter evaluation is imperative to monitor the approved medicines in order to adequately assess the quality, therapeutic effectiveness and safety of medicines user. This study was carried out to evaluate the quality control parameters of 15 different batches of 5 different brands of Paracetamol tablets available in Bangladesh market by means of weight variation test, friability test, hardness test, and disintegration test. Sample brands were ACE, FAST, XCEL, XPA and SERVIGESIC. Paracetamol is one of the over the counter drugs which is most commonly used in Bangladesh. Over the counter drugs are medicines that may be sold directly to a consumer without a prescription from healthcare professionals. Paracetamol is used as an analgesic and antipyretic, in the treatment of a wide variety of arthritic and rheumatic conditions involving musculoskeletal pain and in other painful disorders such as headache, dysmenorrheal and neuralgia. It is also indicated as an analgesic and antipyretic in diseases accompanied by generalized discomfort or fever, such as the common cold and other viral infections (IARC, 1990). As the sales of this widely used drug is not restricted so it is very important to maintain the quality of this drug especially in developing countries like Bangladesh where counterfeit and substandard drugs have become a major challenge to health care services. Today counterfeit and substandard medicines become a major cause of morbidity, mortality, and diminished public

confidence in drugs and health structures in our country (Chandrasekaran 2011). Hope that the quantitative and qualitative data obtained from this study will help in findings some of the lacking in the quality of the available paracetamol tablet in Bangladesh pharma market and in turn it will help in the development of better quality medicine.

Table 1: Physical appearances of collected sample

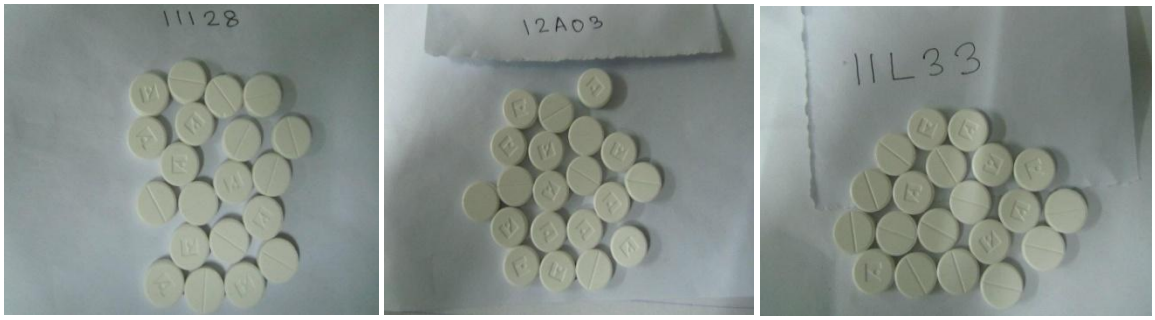
Brand	Color	Shape	Scoring	Logo
ACE	White	Cylindrical	Yes	Yes
FAST	White	Oval	Yes	Yes
XCEL	Pink	Rectangle	Yes	No
XPA	White	Round	Yes	Yes
SERVIGESIC	White	Round	Yes	Yes

1.2.1 ACE

1.2.2 FAST

1.2.3 XCEL

1.2.4 XPA



1.2.5 SERVIGESIC

1.3 Paracetamol:

Paracetamol, known as acetaminophen in the USP and its common name derives from the full chemical name: Para-acetyl-amino-phenol, with the chemical formula $C_8H_9NO_2$ and a molecular weight of 151.16 (McNeil, 2010). Synonyms of paracetamol: 4'- hydroxyacetanilide, Tylenol, paracetamo, paracetamolo, paracetamole, p-acetamidophenol, acetaminofen, p-acetaminophenol (IARC, 1990).

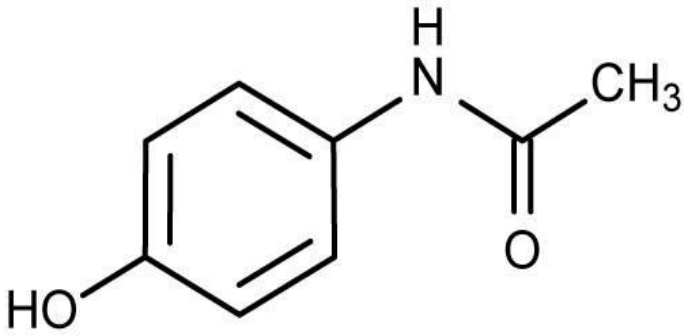


Figure 1: Chemical Structure of Paracetamol

Paracetamol had been synthesized by Morse in 1878 and was first used in medicine by von Mering in 1893 (Bertolini *et al.*, 2006). It is a white, odorless crystalline powder with a bitter taste, soluble in 70 parts of water, 13 parts of acetone, 50 parts of chloroform, 10 parts of ethanol, 40 parts of glycerin, 10 parts of methanol, or 9 parts of propylene glycol. The pKa of acetaminophen is approximately 9.5 at 25^0 C. The octanol/water partition coefficient (log p) of acetaminophen is 0.46. In the solid state, acetaminophen is stable at a moderately elevated temperature (45^0C) when exposed to light, and in moderate humidity. In aqueous solution, acetaminophen is most stable between p^H 4 and 7 at 25^0 C (McNeil, 2010). Paracetamol is generally safe and well tolerated for human use at recommended doses. It also has a low incidence of gastrointestinal side effects at therapeutic doses in contrast to the NSAIDs (Nayak, 2010).

1.4 Methods:

The study is done by means of weight variation test, hardness test, friability test and disintegration test. Weight variation test is very important because it has a relationship with content uniformity of a solid dosage forms. A small weight variation ensures good content uniformity between dosage units; a large weight variation does not ensure good content uniformity. Any of the following factors, can produce excessive tablet variations: (1) poor

granulation flow properties, resulting in uneven die fill; (2) a wide variation in granulation particle size, which result in a variation in die fill density as a function of particle size and particle size distribution at different points in the production run, (3) difference in lower punch length, which result in different size die cavities (Gilbert & Neil, 1986).

Another test carried out is hardness test. Tablet hardness is usually expressed as the load required crushing a tablet placed on its edge. Hardness is thus sometimes termed the tablet crushing strength. The crushing strength test is undertaken to determine the ability of the tablets to withstand pressure during handling, packaging and transportation. Tablet hardness, in turn, influences tablet friability and disintegration time. It usually affects drug dissolution and release and it may affect bioavailability (Lewis, 1960).

Friability is another important quality control parameter and thus the friability test is also carried out. The forces that most often cause tablets to chip, cap or break are known as friction and shock. The friability test is closely related to tablet hardness and is designed to evaluate the ability of the tablet to withstand abrasion in packaging, handling and shipping. The value is expressed as a percentage. A maximum weight loss of not more than 1% of the weight of the tablets being tested during the friability test is considered generally acceptable (Seitz, 1965). Disintegration test is also carried out since disintegration is the most important step of a drug being better dissolution. The breakdown of a drug within its optimum time is the prerequisite for better absorption and consequently better therapeutic action. Disintegration time may vary considering to its disintegrator used. Higher the disintegration time required lower the dissolution rate and followed to poor absorption (Lewis, 1960). So disintegration is the crucial part of a drug for therapeutic action.

1.5 Pharmacokinetics of Paracetamol:

After oral administration, paracetamol is absorbed rapidly from the small intestine, while absorption from the stomach is negligible. The rate of absorption depends on the rate of gastric emptying. The co-administration of food has been shown to slow the rate of absorption of paracetamol. Prokinetic drugs such as metoclopramide accelerate gastric emptying, enhancing the rate of absorption, while drugs that decrease the rate of gastric emptying e.g. morphine slow absorption, and in some cases prevent attainment of therapeutic plasma levels (Forrest, 1982). First-pass metabolism of paracetamol is dose-dependent. Paracetamol is not significantly bound to plasma proteins, and has a volume of distribution of 0.7–1 l kg^{-1}. It is non-ionized at physiological pH and freely crosses the placenta and blood–brain barrier. One gram of propacetamol provides 0.5 g paracetamol after hydrolysis. The minimum plasma paracetamol level required for analgesia and antipyresis is thought to be 10 $\mu g.ml^{-1}$, and although not clearly defined, the therapeutic range is usually stated to be 10–20 $\mu g.ml^{-1}$. 150 $\mu g.ml^{-1}$ is considered to be the threshold for potential hepatotoxicity. Metabolism of paracetamol occurs primarily in the liver, while elimination occurs almost entirely through the kidney. The major urinary metabolites (the glucuronide, sulfate and 3-mercapto derivatives) are observed in most species, although the percentages of these conjugates excreted in urine vary widely among species (Oscier, 2008). A minor but important metabolic pathway involves the conversion of paracetamol to a reactive metabolite by the hepatic cytochrome P450-dependent mixed-function oxidase system shown in fig 2. *N*-Acetyl-*para*-benzoquinone imine was found to be formed as an oxidation product of paracetamol by purified P450. The reactive product was rapidly reduced back to paracetamol by a variety of reductants. Attempts to produce *N*-acetyl-*para*-benzoquinone imine from NADPH and microsomes were not successful owing to this rapid reduction;

however, both purified *N*-acetyl-*para*-benzoquinone imine and paracetamol with an NADPH generating system bound covalently to mouse liver microsomal protein. A subsequent reaction of *N*-acetyl-*para*-benzoquinone imine was found to be conjugation to glutathione, resulting in 3-*S*-glutathionylparacetamol. A correlation has been found between species sensitivity to the hepatotoxicity of paracetamol and the balance between two pathways: (i) formation of glutathione conjugates and the corresponding hydrolysis products (indicative of the 'toxic' pathway) and (ii) metabolism via formation of glucuronide and sulfate esters (the 'detoxification pathway'). At sufficiently high doses of paracetamol, glutathione is depleted and the reactive metabolite binds covalently to cell macromolecules. It has also been noted that paracetamol and *N*-acetyl-*para*-benzoquinone imine may exert their cytotoxic effects via disruption of Ca^{2+} homeostasis secondary to the depletion of soluble and protein-bound thiols. Prostaglandin *H* synthase catalysed the arachidonic acid-dependent polymerization of paracetamol and, in the presence of glutathione, also catalysed the formation of 3-(glutathion- *S*-yl)paracetamol. These reactions involved the overall 1- and 2-electron oxidation of paracetamol via formation of *N*-acetyl-*para*-benzosemiquinone imine and *N*-acetyl-*para*benzoquinone imine . The polymerization reaction was also observed when cumene hydroperoxide was added to microsomes and paracetamol. These data indicate that oxidative or free-radical reactions initiated by paracetamol play a role in the hepatotoxicity of this drug. Paracetamol is activated in the kidney by an NADPH-dependent cytochrome P450 to an arylating agent, which can bind covalently to cellular macromolecules. Studies in several species have suggested that formation of *para*-aminophenol may be of importance in the nephrotoxicity of paracetamol (IARC, 1990).

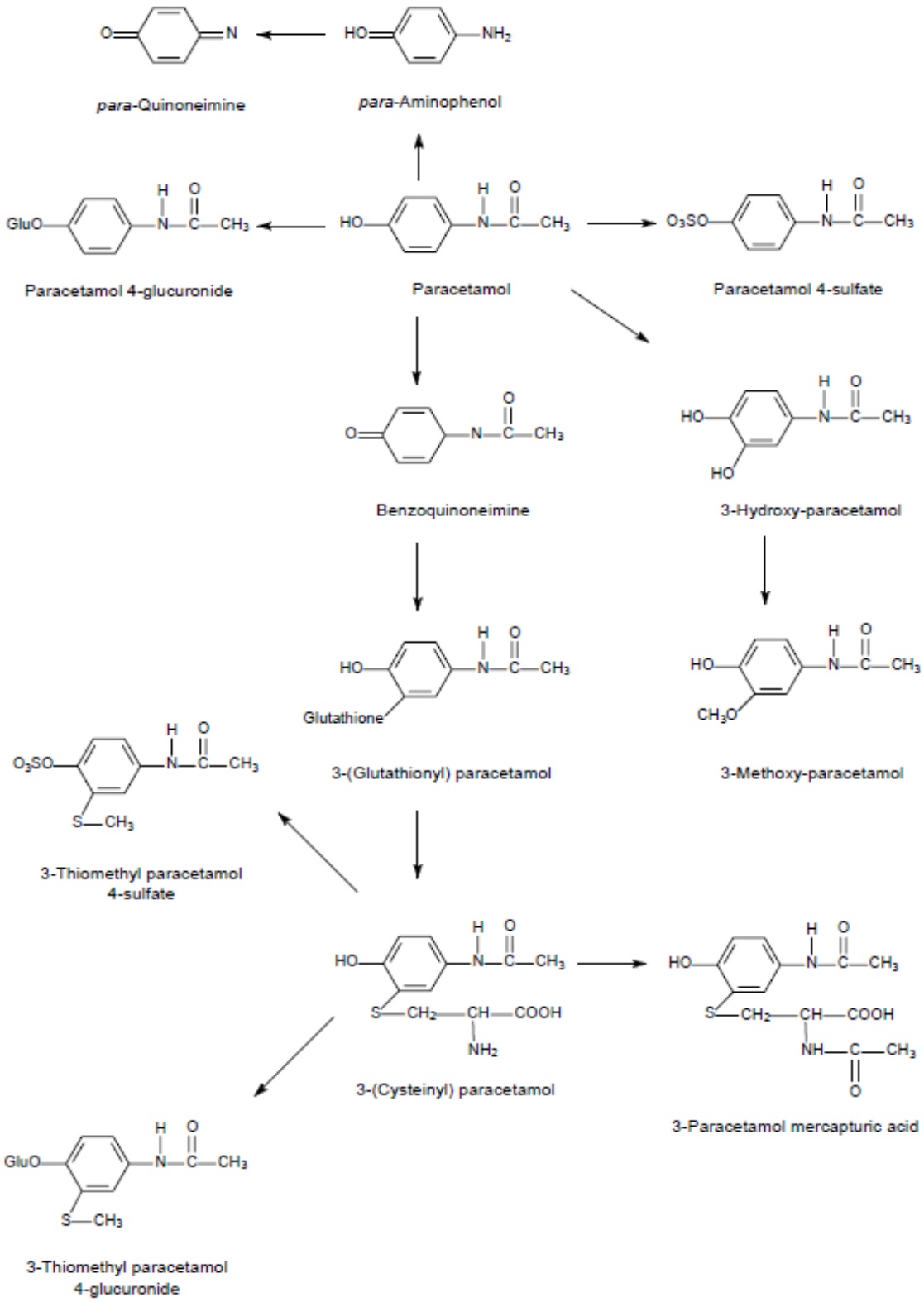


Figure 2: Metabolic Pathway of paracetamol

Elimination half-life is 2–4 h in normal adults, increasing to 4–5 h in newborns and to 11 h in premature infants (Oscier & Milner, 2009).

1.6 Route of administration:

The onset and duration of analgesic action of paracetamol is determined to a large extent by the route of administration. Intravenous administration will achieve therapeutic plasma concentrations within 20 min of an initial dose, and concentrations remain therapeutic for around 2 h post dose. In a comparison of oral and intravenous paracetamol, infusion provide significantly faster onset of analgesia than oral paracetamol, with reduced time until meaningful pain relief. Rectal absorption is slower and more variable than with intravenous or oral administration (Oscier & Milner, 2009).

1.7 Doses of Paracetamol:

Adult dose:

Two 500mg tablets (i.e., 1gm paracetamol) every four to six hours, not exceeding eight tablets (4gms) in any 24 hour period.

Children dose:

a) 2 month old child: single dose of 60mg (i.e. 2.5mL paracetamol liquid at a strength 120mg/5 mL) paracetamol may be given on a doctor's recommendation.

b) Under 3 months: 10mg paracetamol per kilogram body weight (5mg/kg if jaundiced), on a doctor's advice only.

c) 3 months to 1 year: Between 60mg and 120mg (i.e. 2.5mL to 5mL of paracetamol liquid (oral suspension) at strength of 120mg/5mL) may be repeated every 4-6 hours to a maximum of 4 doses in 24 hours.

d) 1 to 5 years: 120mg to 250mg (i.e. 5mL to 10mL of paracetamol liquid (oral suspension) at a strength of 120mg/5mL) may be repeated every 4-6 hours to a maximum of 4 doses in 24 hours.

e) 6 to 12 years: 250mg to 500 mg (i.e. 5mL to 10mL paracetamol liquid (oral suspension) at a strength of 250mg/5mL) may be repeated every 4-6 hours to a maximum of 4 doses in 24 hours.

In general, children's dosages vary with the age of the child and the type of product, therefore the instructions on the pack should always be followed. In general, children's dosages are based on a single dose of 10mg paracetamol per kilogram bodyweight, which can be repeated 4-6 hourly, not exceeding four doses per 24 hours (Paracetamol Information Centre, n.d.b).

1.8 Pharmacology of Paracetamol:

Acetaminophen is a non prescription drug commonly used as a aspirin substitute because it does not cause nausea, vomiting or GI bleeding and it does not interfere with blood clotting. It is equal to aspirin in analgesic and antipyretic effect, but it lacked anti-inflammatory activity.

Acetaminophen inactivate cyclooxygenase enzyme (COX) required for the formation of prostaglandins. This action inhibits the formation of prostaglandins and thereby inhibits their effects on body tissues. The anti prostaglandin effect is considered the primary mechanism of action of acetaminophen activity (Smith, 2009).

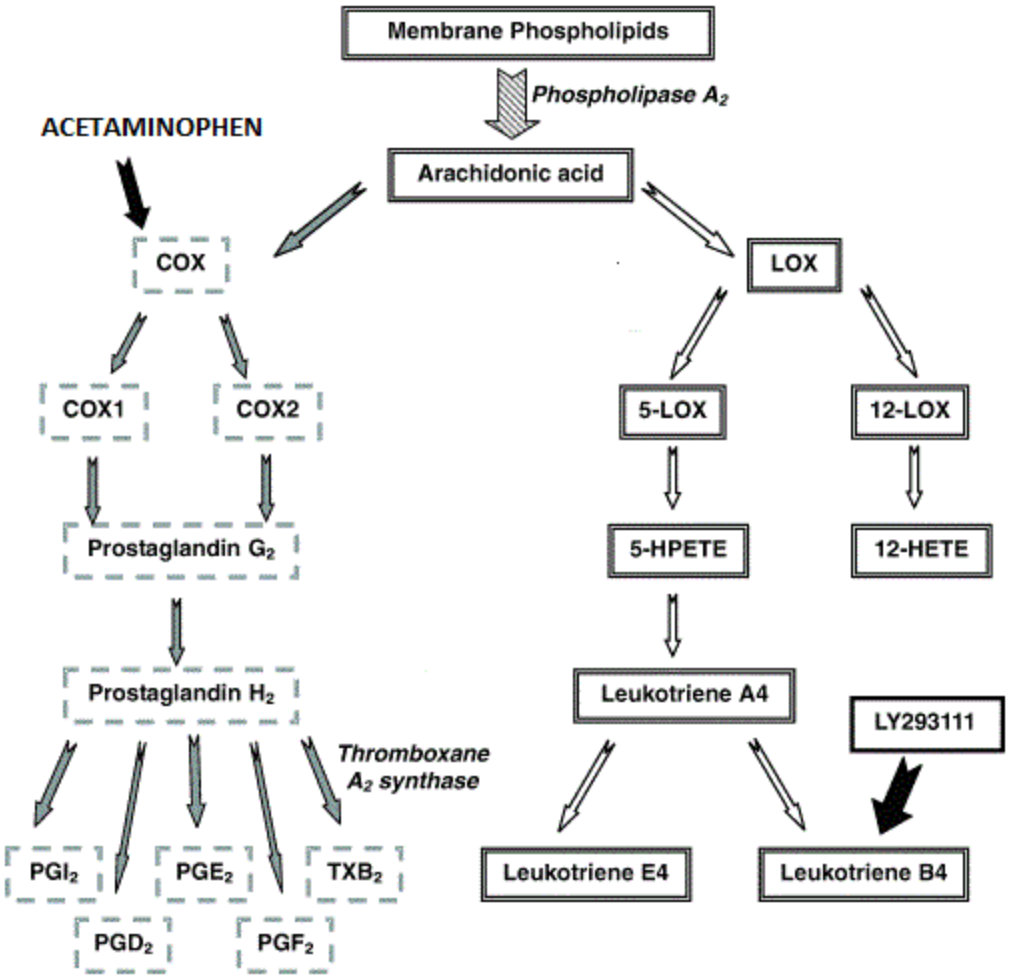


Figure 3: Inhibition of cyclooxygenase enzyme by acetaminophen

1.8.1 Mechanism of action of Acetaminophen as Analgesic:

Potential Mechanisms of APAP (Acetaminophen) Induced Analgesia:

Although suspected for many years, it is now becoming clearer that the mechanisms, which are largely responsible for acetaminophen's analgesic effects are largely central in origin.

The efficacy of systemic (oral) and intrathecal (IT) applications of acetaminophen in preventing the development of hyperalgesia induced through the direct activation of pro-analgesic spinal receptors. Spinal administration of substance P (SP, 30 nmol, IT) in rats produced a decreased thermal threshold, indicating centrally mediated hyperalgesia. Pretreatment of rats with oral acetaminophen (300 mg/ kg), but not vehicle, significantly attenuated IT SP induced

hyperalgesia. Acetaminophen given IT also produced a dose-dependent (10 – 200 μg) antinociceptive effect. In addition, oral APAP suppressed spinal PGE2 release evoked by IT SP in an in vivo IT dialysis model. The ability of IT as well as oral APAP to reverse this spinally initiated hyperalgesia emphasizes the likely central action and bioavailability of the systemically delivered drug.

For the systemic route of delivery, the observation that acetaminophen reversed that centrally mediated hyperalgesia is consistent with its known ability to penetrate into the brain at a dose which failed to alter the acute thermal threshold. This emphasizes that the site of systemic drug action was within the neuraxis via mechanisms that mediate spinal sensitization. Similarly, the oral dose of APAP required to produce a central antihyperalgesic effect was 1,000 times the dose required when administered intrathecally. It is therefore unlikely that the spinal effect of the IT drug effect was due to redistribution of the drug into the periphery. Multiple mechanisms may contribute to the analgesia provided by APAP.

LPS-induced hyperalgesia in the formalin second phase may be involved in the SP-sensitive neuronal pathways, in which the hyperalgesic response elicited by LPS is attenuated by APAP with supraspinal pain modulatory mechanisms (Smith, 2009).

APAP and the Cannabinoid System:

The discovery of involvement of cannabinoid system on pain modulation has opened new mechanistic perspectives. Anandamide and 2-arachidonoylglycerol, 2 endogenous ligands of CB1 and CB2 receptors, mainly metabolized by the fatty acid amide hydrolase, and the monoacylglycerol lipase, respectively, induce antinociceptive effects. Similarly, activation of this system by exogenous ligands for cannabinoid (particularly CB1) receptors induces antinociception in various acute pain tests in rodents but also in several animal models of chronic

pain. Several studies reported that cerebral injection of cannabinoids in the periaqueductal gray or the rostroventral medulla (RVM) elicits antinociception, suggesting the modulation of descending pathways to inhibit pain processing at the spinal level.

APAP could be metabolized in the brain into AM404, and then inhibit the reuptake of anandamide, with subsequent stimulation of CB1 receptors via FAAH. Thus, the antinociceptive activity of APAP may rely on an interaction with the endocannabinoid system. The interaction of APAP with the endocannabinoid system could be on the basis of the reinforcement of the serotonergic system. The observation of the striking structural similarity between APAP and the fatty acid amide N-arachidonoyl-phenolamine (AM404). APAP, following deacetylation to its primary amine (p-aminophenol) is conjugated with arachidonic acid in the brain and spinal cord to form AM404 (via FAAH), which also catalyzes the hydrolysis of anandamide and which can also act in the reverse direction and catalyze the synthesis of anandamide from ethanolamine and arachidonic acid. FAAH can indeed synthesize AM404 from p-aminophenol and arachidonic acid. The analgesic activity of APAP involves potentiation of the cannabinoid/vanilloid tone in the brain and in dorsal root ganglia.

APAP does not bind to CB1 receptors but rather activates CB1 receptors via an indirect pathway relying on FAAH-dependent AM404 formation and subsequent AM404 effects on anandamide transport (Smith, 2009).

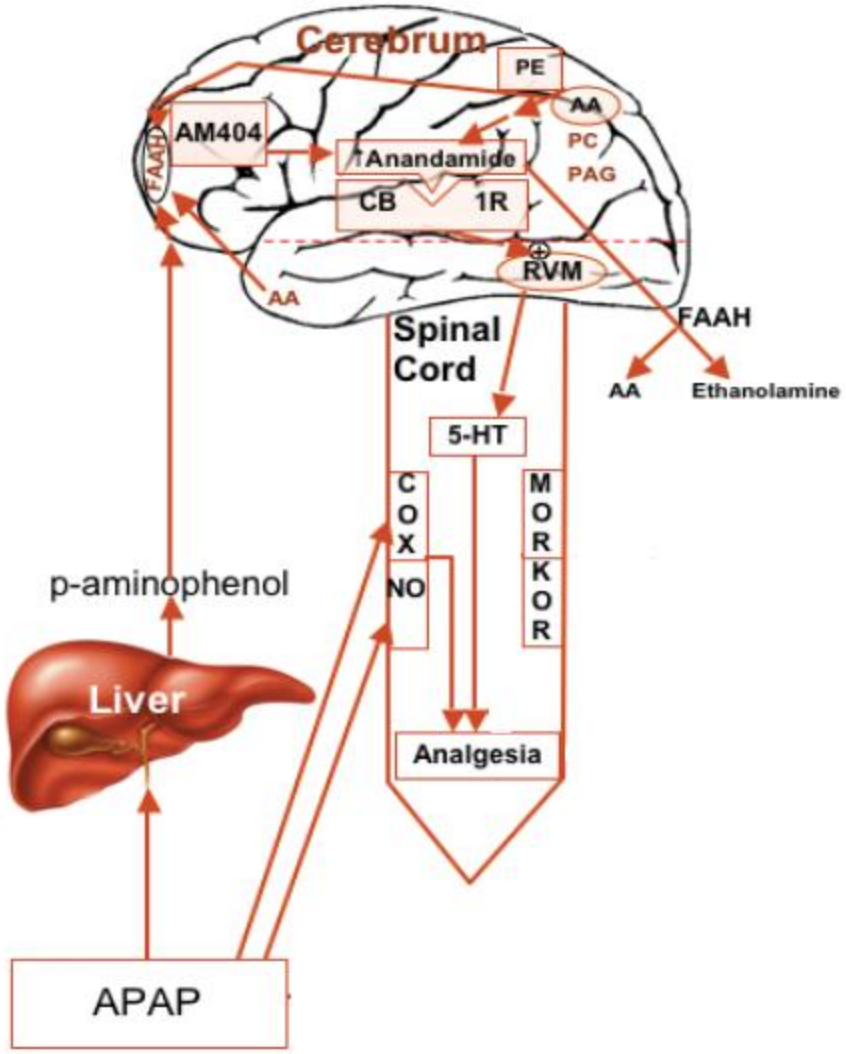


Figure 4: Potential analgesic mechanisms of APAP.

1.8.2 Mechanism of action of Acetaminophen as Antipyretic:

Actaminophen work as antipyretic agent by inhibiting PGE2 in the fever pathway. Fever is mainly occurred by the pathway shown in figure 5. In the pathway of the fever acetaminophen inhibit PGE2 and triggers to reduce the set point of hypothalamus by reducing the temperature of the body (Helsinki, 2006).

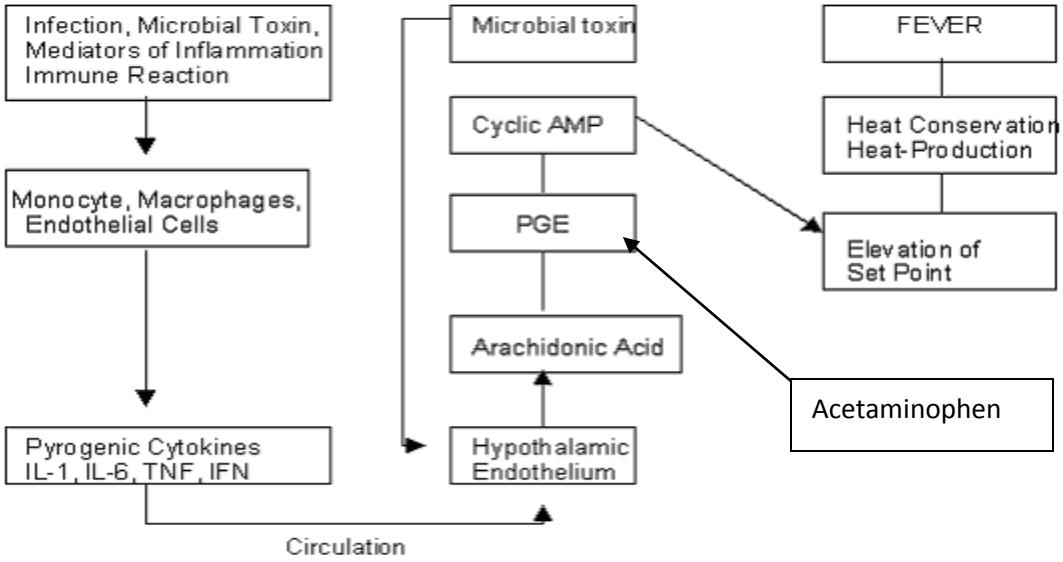


Figure 5: Pathogenesis of fever.

1.8.3 Mechanism of action of Acetaminophen as Antiplatelet activity:

Paracetamol is usually considered not to influence platelet function based on studies on oral paracetamol. However, paracetamol has been shown to inhibit platelet aggregation and production of TxB2 in several studies shown in fig 6. A high dose of Paracetamol inhibits platelet function *in vivo* (Helsinki, 2006). The pathway by which platelet signal is given below:

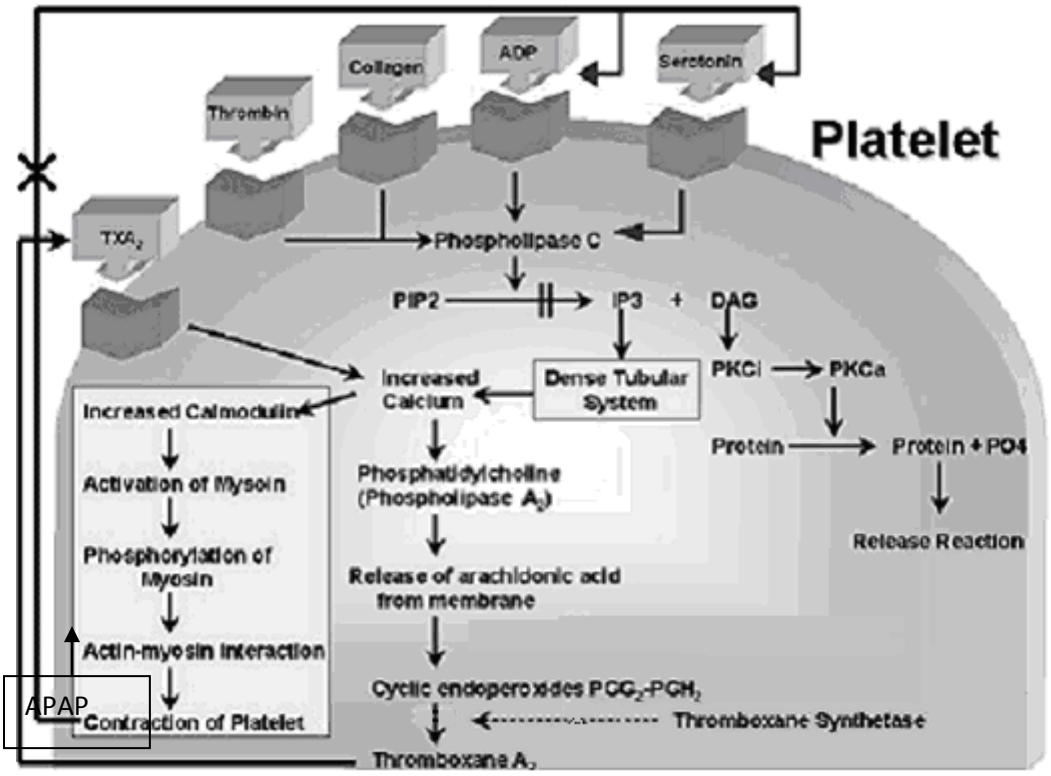


Figure 6 : Platelet signaling pathway.

Acetaminophen inhibits TXA_2 in the platelet signaling pathway. Thus it prevents the platelet aggregation.

1.8.4 Mechanism of action of Acetaminophen as Anti-inflammatory:

Acetaminophens do not act as an anti-inflammatory agent due to the presence of different types of peroxides present in the inflammatory region which in turn inactivates the acetaminophen activity by oxidizes acetaminophen (Helsinki, 2006).

1.9 Toxicity of Paracetamol:

Paracetamol is very well tolerated. The rate of adverse effects is not very significant. Although the major concern with paracetamol administration relates to the potential for hepatotoxicity, this is extremely rare following therapeutic dosing. Therapeutic doses of paracetamol do not

exacerbate stable chronic liver disease, and metabolism of paracetamol is normal in normal patients. In patients with severe disease, however, the elimination half-life can be prolonged. There is debate as to whether therapeutic doses of paracetamol can cause hepatotoxicity or not. In patients with a high alcohol intake, the possibility of hepatotoxicity increase. There is a consensus that overdose in a chronic alcohol abuser may result in more severe hepatotoxicity than in the non-alcoholic. On the other hand very few clinically significant drug interactions with paracetamol have been observed. Co-administration of paracetamol with drugs that induce the cytochrome P450 system (e.g. rifampicin, carbamazepine) increases the risk of drug interaction (Oscier & Milner, 2009).

2.1 Market Survey:

Table 2: Value in BDT, % market share & growth, sold unit/ year of each brands

Brand	Company	Value in BDT	Share %	Growth %	Sold Unit/Year
ACE	Square	259,386,119	12.76	16.64	10,429,144
FAST	ACM	48,429,267	2.38	32.83	2,081,591
XCEL	A-I	19,374,513	0.95	37.43	907,113
XPA	ATP	17,091,178	0.84	30.42	891,750
SERVIGESIC	SDZ	3,379,384	0.17	108.43	10,921

According to the survey conducted by Intercontinental marketing services (IMS), 2nd quarter, 2011 (April-June), (Tablet 2), among these five brand ACE has the highest market share and SERVIGESIC has the lowest market share.

Chapter -2

Literature Review

A study has been performed on evaluation of Acetaminophen tablets by control test. In this study Acetaminophen tablets was prepared using different disintegrants (sodium carboxy methyl cellulose, corn starch, veegum, Avicel 101) at four different hardness for each formulation and weigh variation, diameter, thickness, friability test were carried out. The result of the weight variation test showed, the tablets were of an average weight of 600 mg which is ± 5% that is within the limits of the percentage deviation allowed by USP for tablets weighing 325 mg or more. The variations that observed in this study was with respect to the standard deviation and coefficient of variation where Each value was the mean of 20 tablets. Then thickness of all tablets was measured. The results showed the deviation in thickness is within ± 5% which was tolerable for the normal manufacturing practices. The variation that observed in this study was with respect to standard deviation and coefficient of variation where each value is the mean of 10 tablets. In this study, tablets of four different hardness were prepared from each formulation. A Monsanto hardness tester was used to determine the hardness. The variation that observed in this study was with respect to the standard deviation, and coefficient of variation. The study of friability of the acetaminophen tablets of different formulation showed a relationship between hardness and friability i.e. greater the hardness of the tablets the lesser was the percentage of friability and this may be due to high compressional force at which the granules are packed strongly together and low degree of crumbling during friability. Here Average hardness of 10 tablets is considered (Ahmed A *et al*., 2011).

Ofonaike J *et.al* has performed a study of the pharmaceutical quality of chloroquine and paracetamol products sold in a major Nigerian "market". They worked to evaluate the the pharmaceutical properties including organoleptics (color, texture, smell and taste), and physicochemical properties (weight, drug content and identification, as well as tablet crushing

strength, disintegration and dissolution) of chloroquine and paracetamol oral products obtained from a major Nigerian drug "market" using a less elaborate sampling procedure. The result showed that twenty one percent of the drug products were not registered where 5 were chloroquine and 2 were paracetamol. The organoletic properties indicated that chloroquine and paracetamol tablets were in conformity with BP standards, and did not vary between countries of origin. The assessment of physicochemical properties of the tablet preparations showed that two "imported" product failed the test. Also, there was a tendency for the "imported" products to have high disintegration time as compared to locally produced chloroquine. The content of chloroquine tablets was found to be within normal range, except for one imported product, which had a percentage that outside the BP range. The disintegration time for all paracetamol tablets was within the pharmacopeial range. While 4 product fail the percent dissolution range. The crushing strengths for chloroquine and paracetamol tablets were found within 7.34 to 13.32 kg and 1.91 to 7.28kg, respectively where minimum requirement is 4 kg. Three local chloroquine products did not conform to this requirement. All liquid preparations of chloroquine and paracetamol were packaged in amber color bottle with an exception of one product which was packaged in a white 2L container. None of the chloroquine syrups and only three paracetamol syrup products met the BP requirements for pH (Ofonaike J *et. al* , 2005).

Alebiowu G *et al* have performed another study on Influence of process variables on release properties of paracetamol tablets. The objective was to quantitatively study individual and interaction effects of the nature of binder (N), binder concentration (c) and relative density of tablet (d) on the disintegration time (DT) and dissolution times, *t*1, *t*50 and *t*90, of paracetamol tablet formulations as well as to study the quantitative effects of pregelatinization of starch binders on these parameters. They prepared native and pregelatinized starch, granules, tablets

and then carried out disintegration and dissolution test and the experiment were performed in a factorial design. The result showed that the values of disintegration and dissolution times of paracetamol tablets were used to calculate the independent and interaction coefficient values. There were both positive and negative influences on the disintegration and dissolution properties of the tablets. Positive influence indicates that a particular parameter has increased while negative influence indicates that the value of the parameter has decreased. The Individual effect showed an increase in relative density of tablets will reduce the rate of penetration of liquid into the interior of the tablets, The higher the binder concentration, the slower the removal since higher concentration would lead to more binding. The Interaction effect reported that all the parameters for native/native, pregelatinized/pregelatinized and native/pregelatinized starch binder combinations, the interactions between N and *c* were generally the highest and those between N and *d* generally the lowest. This suggests that a change in the binding agent would have considerable influence on the effects the binder concentration will have on the tablet parameters studied. Thus, the type of starch used as binder is important in formulation studies. there were considerable interactions between the concentration of binder, *c*, and the other two variables N and *d*. This is due to three reasons: first, Plasto-elastic nature of the starch binder, second, extensive plastic deformation under high compressional forces to form strong solid bonds between particles and third, the number of bonds formed depending considerably on the concentration of the binder (Alebiowu G *et al*, 2006).

Eichie E. F *et al*. have performed a research on the effect of particle size of granules on some mechanical properties of paracetamol tablets. Evaluation of the effect of particle size distribution of paracetamol granules on some tablet mechanical properties of paracetamol tablets was their main concern. Tablets were prepared with different sizes granules and the packing fraction of the

tablets from each size fractions was computed and the mean fracture load was used to calculate the tensile strength (T). Finally the result report that an increase in particle size led to a corresponding increase in the packing fraction of the tablets, an increase in granule size brought a slight decrease in T values and this is related to the decrease in particle surface area for contact and cohesion. The study also experience that a general increase in the granule sizes brought about a decrease in the particle density and an increase in the percentage porosity of the tablets and an increase in the granule sizes brought about a corresponding decrease in the friability of the tablets (Eichie E. F *et al*., 2009).

Gangwar S *et al.* have performed a study to compare the disintegrating property of Papaya starch and Sago starch in paracetamol tablets. The extracted Papya and sago starch, evaluate and calculate the swelling power, paste clarity, prepared tablets and carried out weight variation test, hardness test, friability test, disintegration test and dissolution test. The results showed that the average weight variation of the formulated tablets was found to be within acceptable limits, the hardness and friability of the tablets was found to be within acceptable limits. Time to release 50% of drug (T50%) and time to release 70% of drug (T70%) were found to be decreased with the increasing concentration of starch. Sago starch shows higher swelling power than papaya starch and hence the disintegrating power of sago starch is more than that of papaya starch. The prepared tablets of paracetamol with papaya and sago starch as disintegrant were evaluated for avg. weight variation, hardness, friability, disintegration, drug content, T50% and T70% and it was observed that disintegration time decreases with the increase in the concentration of starch and at the equal concentration of both starch, sago starch possess greater disintegrant property (Gangwar S *et al*., 2010).

Ngwuluka N *et al* have carried out an extensive study on formulation and evaluation of paracetamol tablets manufactured using the dried fruit of *Phoenix dactylifera Linn* as an excipient. The researcher's objective was to evaluate dried date palm fruit as a pharmaceutical excipient and to check its impact on quality control tests that included uniformity of weight, hardness, friability, disintegration and dissolution of tablets. They prepared date palm powder and the batches of paracetamol tablets formulated by using it as excipicents. The volume of granules, the flow rate of granules and the angle of repose was determined and finally the batches of tablets were evaluated by Compendial and non-compendial test to assess the quality and performance of the batches with different binders in comparison with one another. The result showed that as USP states that for tablets weighing more than 324 mg, weights of not more than two tablets should deviate from the average weight by more than 5% . The tablets from the different batches which had different binders and at different concentrations met the compendial specification. The mechanical strength of a tablet determines the disintegration time and the rate of dissolution. As the concentration of the binder increases, the mechanical strength increases. The minimum satisfactory mechanical strength of a tablet is 4 kg. Acacia and tragacanth did not comply with the specification. All the concentrations of date palm met the specifications implying that date palm produced tablets with good mechanical strength. These study also showed that paracetamol tablets prepared with acacia and tragacanth were friable though hard as the concentration of the binder increases. 2% tragacanth could not withstand the friability test due to its softness. On the contrary, the friability of the tablets prepared with date palm decreases as the concentration of the binder increases. However, only 20% date palm met the compendial specification for friability. Although, the batches of the different types and concentrations of binders contained the same quantity of disintegrant , only tragacanth at its different

concentrations met the BP specification for disintegration which states that uncoated tablets should disintegrate within 15 min. While, 2 and 5% acacia disintegrated in less than 30 min, none of the concentrations of date palm disintegrated in less than 30 min. The USP and BP states that the quantity of drug released should not be less than 85% of the labeled amount of paracetamol in 30 min. In these study all the batches of date palm and acacia complied with the specification (Ngwuluka N et al , 2010).

Chandrasekaran A *et al*. have performed a study on post–market in vitro equivalency evaluation of Paracetamol tablets. The researcher's objective was evaluation of paracetamol tablets (500mg) of different brands by specific quality control test. The used six different brand of paracetamol tablets and carried out weight variation test, hardness test, friability test and disintegration test. Uniformity of weight, disintegration are compendial standards to assess the quality of tablets while hardness and friability are referred to as non-compendial standards although friability is now included in the USP, 1995. In weight variation test the result showed that all of the brands complied with the USP specification. The compendia specification for friability is 1% and friability for all brands was below 1%. The tablets of all brands were satisfactory for hardness where the standard for the hardness test is a 4 kg/square inch gauge. From the research carried out, they have found that one product showed 96.23%, and the other showed 88.03%, 95.26%, 97.49%,93.75% and 96.41% of the drug released at 30 min where according to USP specification, paracetamol tablets should release more than 80% of drug at 30 min. So the results complied with the USP specification (Chandrasekaran A et al., 2011).

Chapter -3

Materials & Methods

3.1 Materials and methods:

3.1.1 Weight variation test:

.Materials: Analytical balance, Tablets.

Table 3: Name and specification of instrument required in weight variation test.

Instrument	Specification
Analytical balance	Electronic Balance (Shimadzu, Japan)

Figure 7: Electronic Balance (Shimadzu, Japan)

Method: The experiment was started with 20 tablets and each tablet was weighed individually. Average weight of all the tablets was taken and considered as the standard weight of the individual tablet. All the tablet was weighed individually and observed whether the individual weight are within the range or not. The tablets meet the USP test if not more than two tablets are outside the percentage limit and if no tablet differ by more than two times the percentage limit (Gilbert S, 1986).

Table 4: Limit of weight variation test (Lachman *et al.*, 1986)

Average Weight	Percentage difference
130 mg or less	±10
More than 130	±7.5
324 mg and above	± 5

3.1.2 Hardness test:

Materials: Hardness Tester, Tablets.

Table 5: Name and specification of instrument required in Hardness test.

Instrument	Specification
Hardness Tester	VEEGO Hardness Tester

Figure 8: VEEGO Hardness Tester

Method: The hardness of 10 tablets was determined by using hardness tester. The lower plunger was placed in contact with the tablets and a zero reading was taken. The plunger was then forced against a spring by tuning a threaded bolt until the tablet fractured as the spring was compressed

a pointer rites along a gouge in the barrel to indicate the force. A force of about 4 kg is considered to be the minimum for hardness where 1 kg =9.81 Newton (Gilbert S, 1986).

3.1.3 Friability test:

Materials: Friability tester, electronic balance, tablets.

Table 6: name and specification of instrument required to friability test.

Instrument	Specification
Friability Tester	VEEGO Friability Tester

Figure 9: VEEGO Friability Tester

Method: The experiment was started by taking a sample of whole 10 tablets and the tablets were carefully dusted prior to testing d then weighed these 10 tablets which were considered as the initial reading. All the tablets were placed in the drum of friability tester and rotate 100 times and removed the tablets. The percentage was calculated. According to USP the tablets should not lose more than 1% of their total weight (B.P. appendix: XVII).

3.1.4 Disintegration test:

Materials: disintegration tester, distilled water, pH meter, 0.1M HCL

Table 7.Name and specification instrument required to disintegration test.

Instrument	Specification
Disintegration tester	Vanguard Pharmaceutical Machinary INC

Figure 10: Vanguard Pharmaceutical Machinary INC

Method: At first, the disintegration tester was assembled. Then 600ml of 0.1 M HCl (pH- 1.2) was placed in each 1000ml beaker (N.B: The volume of the liquid was such that when the assembly is in the highest position the wire mesh was at least 15mm below the surface of the liquid and when the assembly was in the lowest position the wire mesh was at least 25 mm above the bottom of the beaker and the upper open ends of the tubes remain above the surface of the liquid). The temperature was maintained at 37^0 C. Then one tablet was placed in each of the 6 tubes and the apparatus was operated for the prescribed period. All the tablets must be disintegrate within the prescribed time. Disintegration is considered to be achieved when no

residues remain on the scree, or if there is a residue, it consists of a soft mass having no palpably firm, unmoistened core, or only fragments of coating (tablets) may adhere to the lower surface of the disc. If one or two tablets fail to disintegrate completely, the test must be repeated on 12 additional tablets.

Table 8: Limit of disintegration time (Lachman *et al.,* 1986).

Type of tablet	Disintegration time
Uncoated tablet	15 minutes
Coated tablet	60 minutes or 1 hour

Chapter -4
Result

4.1 weight variation test:

Table 9: Weight Variation test of 3 batches of ACE Tablet

BRAND	Tab no.	Batch# 1100304 Weight(g)	Weight variation (%)	Batch# 1100274 Weight(g)	Weight variation (%)	Batch # 1110202 Weight(g)	Weight variation (%)
ACE	1	0.58	0	0.58	-1.72	0.58	0
	2	0.58	0	0.58	-1.72	0.58	0
	3	0.57	1.75	0.55	3.64	0.58	0
	4	0.58	0	0.57	0	0.58	0
	5	0.58	0	0.58	-1.72	0.58	0
	6	0.58	0	0.57	0	0.58	0
	7	0.58	0	0.57	0	0.58	0
	8	0.57	1.75	0.55	3.64	0.58	0
	9	0.58	0	0.58	-1.72	0.58	0
	10	0.59	-1.69	0.58	-1.72	0.57	1.75
	11	0.58	0	0.57	0	0.58	0
	12	0.57	1.75	0.57	0	0.58	0
	13	0.58	0	0.57	0	0.58	0
	14	0.58	0	0.56	1.79	0.58	0
	15	0.58	0	0.56	1.79	0.59	-1.69
	16	0.57	1.75	0.59	-3.39	0.58	0
	17	0.58	0	0.57	0	0.59	-1.69
	18	0.56	3.57	0.57	0	0.58	0
	19	0.57	1.75	0.57	0	0.58	0
	20	0.57	1.75	0.59	-3.39	0.58	0

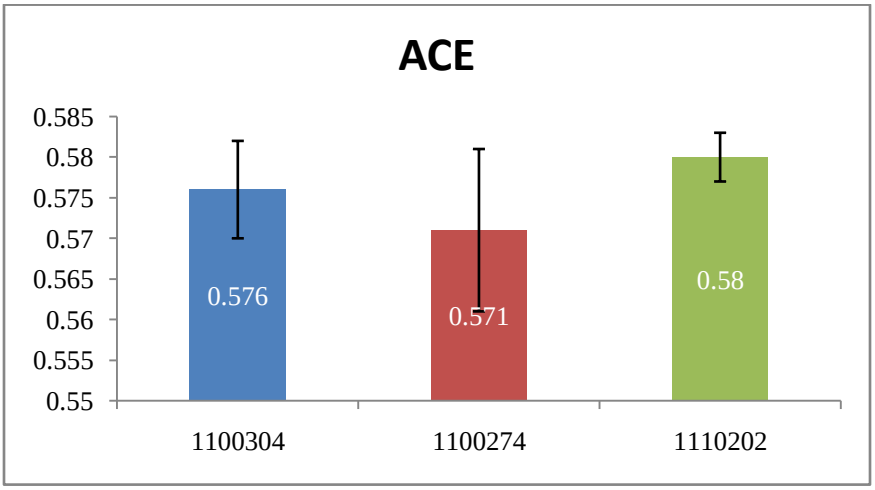
The weight variation of three different batches of Ace tablet: Batch No-1100304 has the average weight of 0.58g. The % weight variation ranged from -1.69 to 3.57%. 1 Batch No- 1100274 has

the average weight of 0.57g. The % weight variation ranged from -3.39 to 3.64%.Batch No 1110202 has the average weight of 0.58g. The % weight variation ranged from -1.69 to 1.75%.

Table 10: Mean weight and standard deviation of the three batches of ACE Tablets

Brand	Batch	Mean weight (g) (n=20)	Standard Deviation
ACE	1100304	0.576	0.006
	1100274	0.571	0.010
	1110202	0.580	0.003

Figure 11: Mean weight and standard deviation of the three batches of ACE Tablets



The mean weight and standard deviation of three batches of ACE tablets. Batch No- 1100304 has mean value 0.576g and standard deviation 0.006. Batch No- 1100274 has mean value 0.571g and standard deviation 0.010. Batch No- 1110202 has mean value 0.580g and standard deviation 0.003.

Table 11: Weight Variation test of 3 batches of FAST Tablet

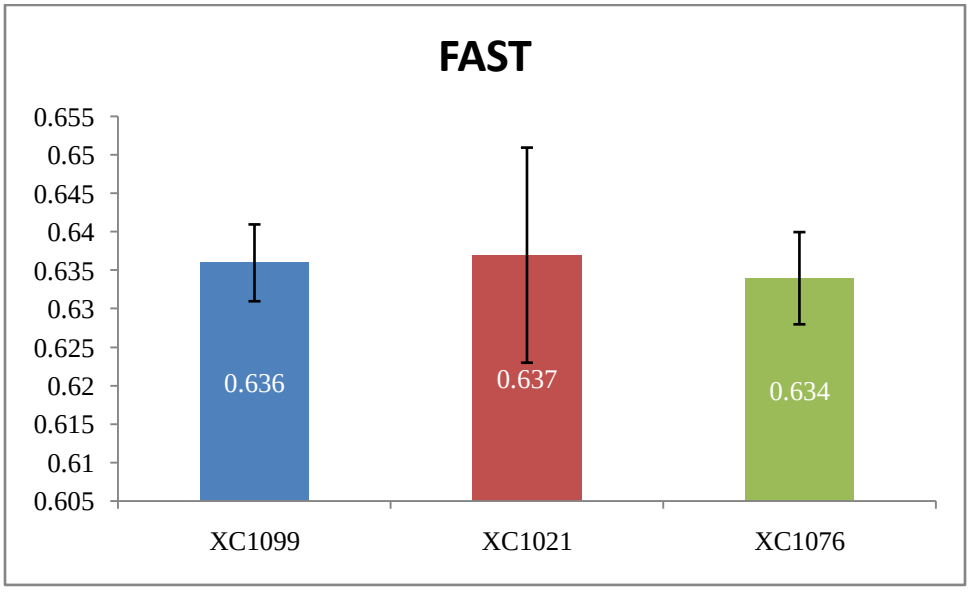
BRAND	Tab no.	Batch# XC1099 Weight(g)	Weight variation (%)	Batch# XC1021 Weight(g)	Weight variation (%)	Batch # XC1076 Weight(g)	Weight variation (%)
FAST	1	0.64	-1.56	0.64	0	0.64	0
	2	0.63	0	0.65	-1.54	0.63	-1.54
	3	0.63	0	0.64	0	0.63	0
	4	0.63	0	0.64	0	0.64	0
	5	0.63	0	0.64	0	0.62	0
	6	0.64	-1.56	0.63	1.59	0.64	1.59
	7	0.63	0	0.64	0	0.64	0
	8	0.64	-1.56	0.68	-5.88	0.64	-5.88
	9	0.64	-1.56	0.62	3.23	0.63	3.23
	10	0.63	0	0.65	-1.54	0.63	-1.54
	11	0.64	-1.56	0.63	1.59	0.64	1.59
	12	0.64	-1.56	0.64	0	0.63	0
	13	0.65	-3.08	0.64	0	0.62	0
	14	0.64	-1.56	0.64	0	0.63	0
	15	0.64	-1.56	0.63	1.59	0.64	1.59
	16	0.63	0	0.62	3.23	0.63	3.23
	17	0.64	-1.56	0.65	-1.54	0.64	-1.54
	18	0.63	0	0.63	1.59	0.64	1.59
	19	0.64	-1.56	0.63	1.59	0.64	1.59
	20	0.64	-1.56	0.61	4.92	0.63	4.92

The weight variation of three different batches of Fast tablets. Batch No XC1099 has the average weight of 0.63g. The % weight variation ranged from -3.08 to 0%. Batch No- XC1021 has the average weight of e 0.64g. The % weight variation ranged from -5.88 to 4.92%. Batch No- XC1076 has the average weight of 0.64g. The % weight variation ranged from -5.88 to 4.92%.

Table 12: Mean weight and standard deviation of the three batches of FAST Tablets

Brand	Batch	Mean weight (g) (n=20)	Standard Deviation
FAST	XC1099	0.636	0.005
	XC1021	0.637	0.014
	XC1076	0.634	0.006

Figure 12: Mean weight and standard deviation of the three batches of Fast Tablets



The mean weight and standard deviation of three batches of FAST tablets. Batch No- XC1099 has mean value 0.636g and standard deviation 0.005. Batch No- XC1021 has mean value 0.637g and standard deviation 0.014. Batch No- XC1076 has mean value 0.634g and standard deviation 0.006.

Table 13: Weight Variation test of 3 batches of XCEL Tablet

BRAND	Tab no.	Batch# LE31 Weight(g)	Weight variation (%)	Batch# KE125 Weight(g)	Weight variation (%)	Batch # OE136 Weight(g)	Weight variation (%)
XCEL	1	0.63	-1.59	0.63	0	0.61	0
	2	0.63	-1.59	0.63	0	0.60	1.67
	3	0.63	-1.59	0.63	0	0.62	-1.67
	4	0.61	1.64	0.63	0	0.60	1.67
	5	0.63	-1.59	0.64	-1.56	0.61	0
	6	0.62	0	0.62	1.61	0.61	0
	7	0.64	-3.13	0.61	3.28	0.60	1.67
	8	0.63	-1.59	0.63	0	0.61	0
	9	0.62	0	0.63	0	0.61	0
	10	0.62	0	0.63	0	0.61	0
	11	0.63	-1.59	0.63	0	0.61	0
	12	0.62	0	0.62	1.61	0.59	3.39
	13	0.61	1.64	0.62	1.61	0.60	1.67
	14	0.64	-3.13	0.62	1.61	0.60	1.67
	15	0.63	-1.59	0.63	0	0.61	0
	16	0.62	0	0.63	0	0.61	0
	17	0.61	1.64	0.62	1.61	0.60	1.67
	18	0.62	0	0.63	0	0.61	0
	19	0.62	0	0.62	1.61	0.61	0
	20	0.62	0	0.62	1.61	0.61	0

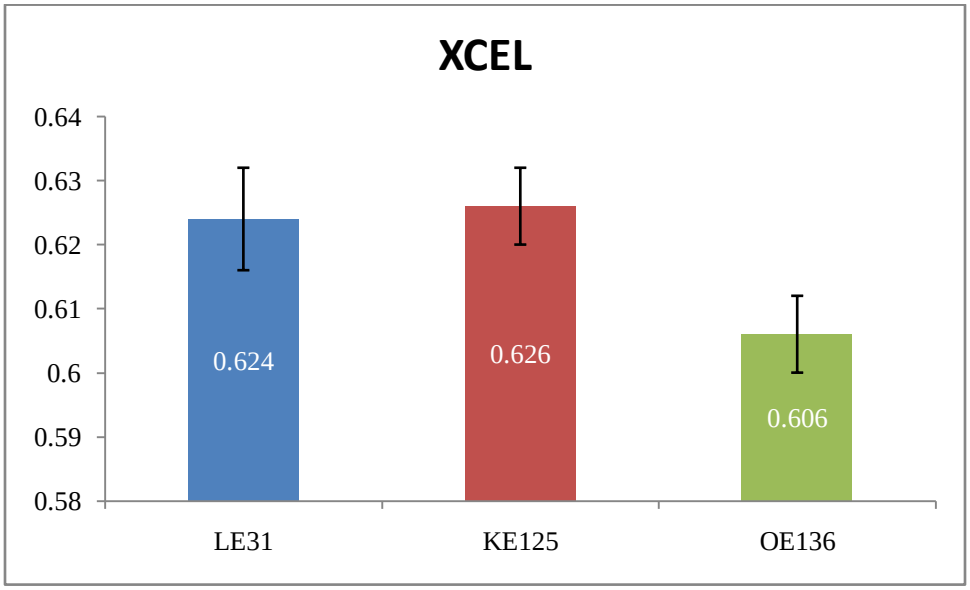
The weight variation of three different batches of Xcel tablet. Batch No -LE31 has the average weight of Xcel 0.62g. The % weight variation ranged from -3.13 to 1.64%. Batch No KE 125 has the average weight of Xcel 0.63g. The % weight variation ranged from -1.56 to 3.28%. Batch

No-OE136 has the average weight of Xcel 0.61g. The % weight variation ranged from -1.67 to 3.39%.

Table 14 : Mean weight and standard deviation of the three batches of XCEL Tablets

Brand	Batch	Mean weight (g) (n=20)	Standard Deviation
XCEL	LE31	0.624	0.008
	KE125	0.626	0.006
	OE136	0.606	0.006

Figure 13: Mean weight and standard deviation of the three batches of Xcel Tablets



The mean weight and standard deviation of three batches of XCEL tablets. Batch No- LE31 has mean value 0.624 and standard deviation 0.008. Batch No- KE125 has mean value 0.626g and standard deviation 0.006. Batch No- OE136 has mean value 0.606g and standard deviation 0.006.

Table 15: Weight Variation test of 3 batches of XPA Tablet

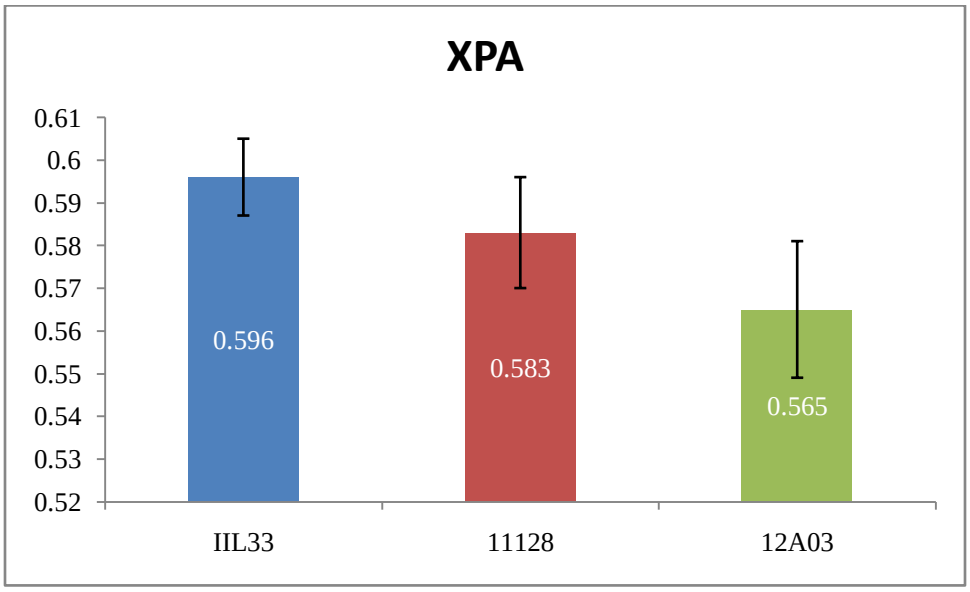
BRAND	Tab no.	Batch# IIL33 Weight(g)	Weight variation (%)	Batch# 11128 Weight(g)	Weight variation (%)	Batch # 12A03 Weight(g)	Weight variation (%)
XPA	1	0.60	0	0.61	-1.64	0.56	7.14
	2	0.59	1.69	0.60	0	0.59	1.69
	3	0.60	0	0.60	0	0.58	3.45
	4	0.60	0	0.59	1.69	0.58	3.45
	5	0.59	1.69	0.59	1.69	0.56	7.14
	6	0.60	0	0.58	3.45	0.55	9.09
	7	0.59	1.69	0.59	1.69	0.58	3.45
	8	0.59	1.69	0.58	3.45	0.58	3.45
	9	0.58	3.45	0.56	7.14	0.58	3.45
	10	0.60	0	0.60	0	0.52	15.38
	11	0.58	1.69	0.58	3.45	0.56	7.14
	12	0.61	-1.64	0.57	5.26	0.57	5.26
	13	0.60	0	0.56	7.14	0.56	7.14
	14	0.60	0	0.58	3.45	0.55	9.09
	15	0.61	-1.64	0.58	3.45	0.57	5.26
	16	0.61	-1.64	0.57	5.26	0.57	5.26
	17	0.59	1.69	0.58	3.45	0.58	3.45
	18	0.60	0	0.59	1.69	0.55	9.09
	19	0.60	0	0.58	3.45	0.55	9.09
	20	0.58	3.45	0.58	3.45	0.56	7.14

The weight variation of three different batches of XPA tablet. Batch No IIL33 has the average weight 0.60g. The % weight variation ranged from -1.64 to 3.45%. Batch No 11128 has the average weight of 0.60g. The % weight variation ranged from -1.64 to 7.41%. 4.3) Batch No 12A03 has the average weight of 0.60g. The % weight variation ranged from 1.69 to 15.38%.

Table 16: Mean weight and standard deviation of the three batches of XPA Tablets

Brand	Batch	Mean weight (g) (n=20)	Standard deviation
XPA	IIL33	0.596	0.009
	11128	0.583	0.013
	12A03	0.565	0.016

Figure 14: Mean weight and standard deviation of the three batches of Xcel Tablets



The mean weight and standard deviation of three batches of XPA tablets. Batch No- IIL33 has mean value 0.596 and standard deviation 0.009. Batch No- 11128 has mean value 0.583g and standard deviation 0.013. Batch No- 12A03 has mean value 0.0.565g and standard deviation 0.016.

Table 17 : Weight Variation test of 3 batches of SERVIGESIC Tablet

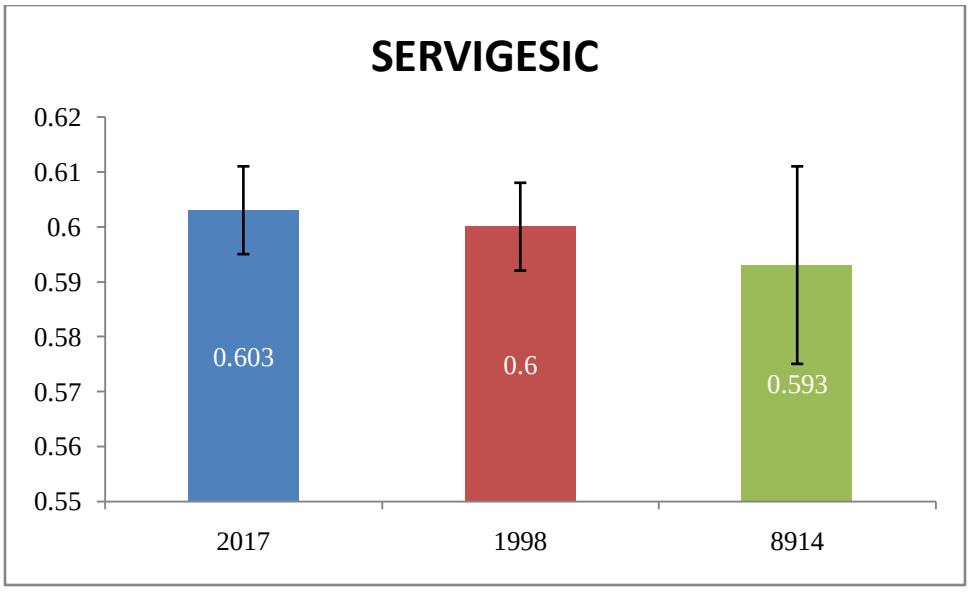
BRAND	Tab no.	Batch# 2017 Weight(g)	Weight variation (%)	Batch# 1998 Weight(g)	Weight variation (%)	Batch # 8914 Weight(g)	Weight variation (%)
SERVIGESIC	1	0.60	0	0.60	0	0.60	-1.67
	2	0.59	1.64	0.61	-1.64	0.59	0
	3	0.61	-1.64	0.60	0	0.56	5.36
	4	0.60	0	0.60	0	0.62	-4.84
	5	0.59	1.64	0.61	-1.64	0.58	1.72
	6	0.61	-1.64	0.60	0	0.60	-1.67
	7	0.61	-1.64	0.59	1.69	0.61	-3.28
	8	0.61	-1.64	0.60	0	0.57	3.51
	9	0.60	0	0.60	0	0.58	1.72
	10	0.61	-1.64	0.58	3.45	0.61	-3.28
	11	0.60	0	0.61	-1.64	0.60	-1.67
	12	0.59	1.64	0.61	-1.64	0.59	0
	13	0.61	-1.64	0.61	-1.64	0.59	0
	14	0.62	-3.23	0.59	1.69	0.61	-3.28
	15	0.61	-1.64	0.60	0	0.58	1.72
	16	0.61	-1.64	0.61	-1.64	0.60	-1.67
	17	0.61	-1.64	0.60	0	0.61	-3.28
	18	0.59	1.69	0.60	0	0.56	5.36
	19	0.60	0	0.59	1.69	0.58	1.72
	20	0.60	0	0.60	0	0.62	-4.84

The weight variation of three different batches of SERVIGESIC tablet. Batch No-2017 has the average weight of 0.60g. The % weight variation ranged from -3.23 to 1.69%. Batch No-1998 has the average weight of 0.60g. The % weight variation ranged from -3.45 to 1.69%. Batch No-8914 has the average weight of 0.59g. The % weight variation ranged from -4.84 to 5.36%.

Table 18: Mean weight and standard deviation of weight of the three batches of SERVIGESIC Tablets

Brand	Batch	Mean weight (g) (n=20)	Standard Deviation
SERVIGESIC	2017	0.603	0.008
	1998	0.600	0.008
	8914	0.593	0.018

Figure 15: Mean weight and standard deviation of the three batches of Servigesic Tablets



The mean weight and standard deviation of three batches of Servigesic tablets. Batch No- 2017 has mean value 0.603 and standard deviation 0.008. Batch No- 1998 has mean value 0.600g and standard deviation 0.008. Batch No- 8914 has mean value 0.0.593g and standard deviation 0.018.

6.1 Hardness test

Table 19: Hardness test of 3 batches of ACE Tablet

Brand Name	Tab No	Hardness (kg)		
		Batch no# 1100304	Batch no# 1100274	Batch no# 1110202
ACE	1	12.1	16.1	12.3
	2	11.6	13.1	16.1
	3	10.7	15.3	16.1
	4	14.1	14.5	15.7
	5	10.7	15.1	16.4
	6	10.3	15.5	17.3
	7	11.3	13.0	11.1
	8	12.4	14.5	15.1
	9	13.5	14.1	15.2
	10	13.6	13.5	14.0

The hardness of the tablets ranged from 10.3 to 14.1kg in Batch No-1100304, 13.0 to 16.1kg in Batch No-1100274 and 11.1 to 17.3kg in Batch No-1110202.

Table 20: Mean hardness and standard deviation of hardness of the three batches of ACE Tablets

Brand	Batch	Mean hardness (kg) (n=10)	Standard Deviation
ACE	1100304	12.03	1.345
	1100274	14.47	1.049
	1110202	14.93	1.933

The mean hardness and standard deviation of three batches of ACE tablets. Batch No- 1100304 has mean value 12.03 and standard deviation 1.345. Batch No- 1100274 has mean value 14.47 and standard deviation 1.049. Batch No- 1110202 has mean value 14.93 and standard deviation 1.933.

Figure 16: Mean hardness and standard deviation of the three batches of ACE Tablets

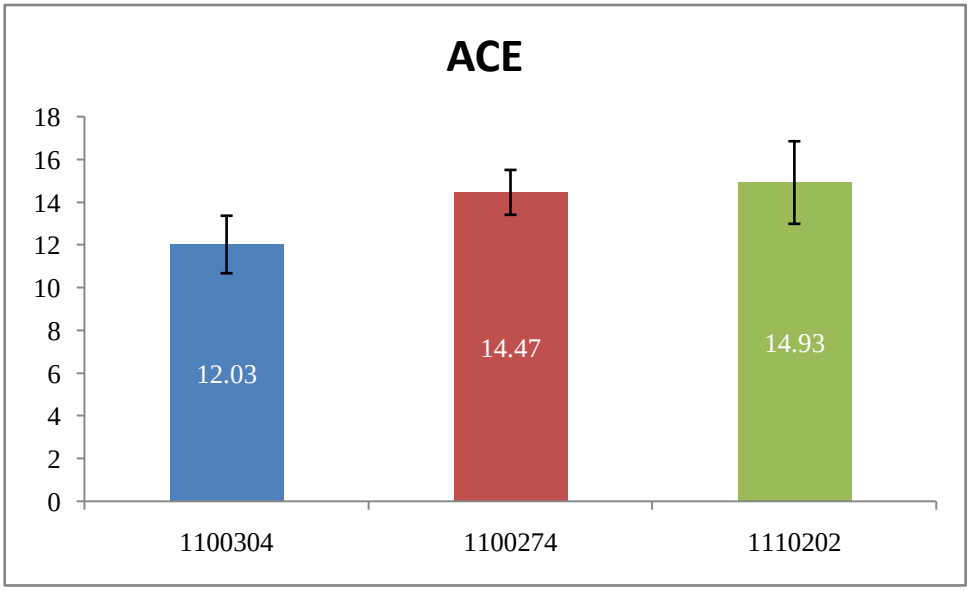


Table 21: Hardness test of 3 batches of FAST Tablet

Brand Name	Tab No	Hardness (kg)		
		Batch no# XC1099	Batch no# XC1021	Batch no# XC1076
ACE	1	15.1	17.9	15.9
	2	15.3	10.2	15.1
	3	18.9	17.2	17.2
	4	16.1	12.7	18.2
	5	18.5	16.3	16.3
	6	13.6	17.0	17.5
	7	18.3	10.5	14.9
	8	10.9	18.4	14.7
	9	15.1	18.7	14.8
	10	14.5	16.5	17.3

The hardness of the tablets ranged from 10.9 to 18.9kg in Batch No-XC1099, 10.2 to 18.7kg in Batch No-XC1021 and 14.7 to 18.2kg in Batch No -XC1076.

Table 22: Mean hardness and standard deviation of hardness of the three batches of FAST Tablets

Brand	Batch	Mean hardness (kg) (n=10)	Standard Deviation
FAST	XC1099	15.63	2.465
	XC1021	15.54	3.199
	XC1076	16.19	1.295

The mean hardness and standard deviation of three batches of FAST tablets. Batch No- XC1099 has mean value 15.63 and standard deviation 2.465. Batch No- XC1021 has mean value 15.54

and standard deviation 3.199. Batch No- XC1076 has mean value 16.19 and standard deviation 1.29

Figure 17: Mean hardness and standard deviation of the three batches of Fast Tablets

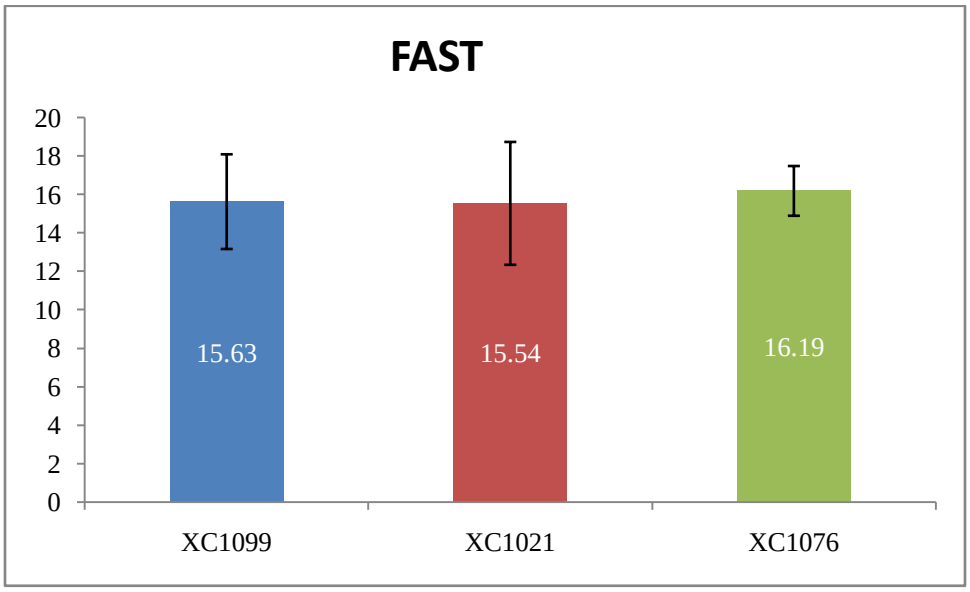


Table 23: Hardness test of 3 batches of XCEL Tablet

Brand Name	Tab No	Hardness (kg)		
		Batch no# LE31	Batch no# KE125	Batch no# OE136
XCEL	1	6.9	14.5	14.0
	2	9.0	11.7	14.8
	3	7.4	16.0	17.1
	4	11.2	12.4	17.6
	5	12.0	10.0	14.6
	6	8.3	15.7	13.7
	7	11.0	16.7	17.8
	8	11.5	12.7	17.4
	9	10.1	16.0	16.0
	10	10.0	10.8	11.8

The hardness of the tablets ranged from 6.9 to 12.0kg in Batch No-LE31, 10.0 to 16.0kg in Batch No-KE125 and 11.8 to 17.8kg in Batch No OE136.

Table 24: Mean hardness and standard deviation of hardness of the three batches of XCEL Tablets

Brand	Batch	Mean weight (g)	Standard deviation
XCEL	LE31	9.74	1.772
	KE125	13.65	2.426
	OE136	15.48	2.0164

The mean hardness and standard deviation of three batches of XCEL tablets. Batch No- LE31 has mean value 9.74 and standard deviation 1.722. Batch No- KE125 has mean value 13.65 and standard deviation 2.426. Batch No- OE136 has mean value 15.48 and standard deviation 2.0164

Figure 18: mean hardness and standard deviation of the three batches of XCEL tablets

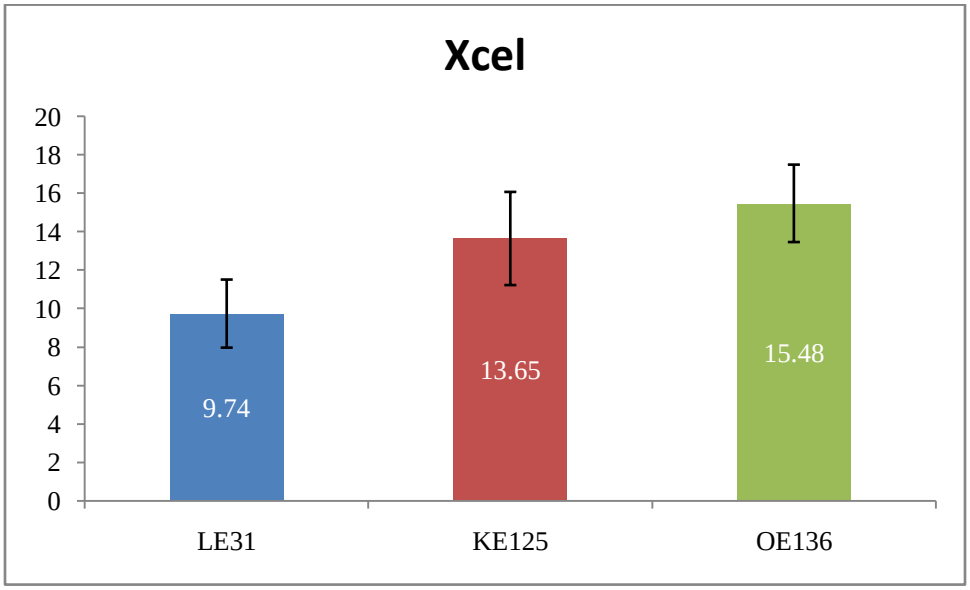


Table 25: Hardness test of 3 batches of XPA Tablet

Brand Name	Tab No	Hardness (kg)		
		Batch no# 11L33	Batch no# 11128	Batch no# 12A03
XPA	1	18.0	15.8	18.9
	2	7.4	16.4	19.0
	3	8.4	.18.6	16.6
	4	19.2	19.2	17.9
	5	10.2	19.2	18.8
	6	7.4	15.8	17.9
	7	18.4	15.8	18.2
	8	7.8	18.0	16.9
	9	18.0	12.8	15.2
	10	7.6	14.8	16.8

The hardness of the tablets ranged from 7.4 to 19.2kg in Batch No-11L33, 12.8 to 19.2kg in Batch No-11128 and 15.2 to 19.0kg in Batch No 12A03.

Table 26: Mean hardness and standard deviation of hardness of the three batches of XPA Tablets

Brand	Batch	Mean weight (g)	Standard deviation
XPA	11L33	12.24	5.372
	11128	16.52	2.394
	12A03	17.62	1.225

The mean hardness and standard deviation of three batches of XPA tablets. Batch No- IIL22 has mean value 12.24 and standard deviation 5.372. Batch No- 11128 has mean value 16.52 and standard deviation 2.394. Batch No- 12A03 has mean value 17.62 and standard deviation 1.225

Figure 19: Mean hardness and standard deviation of the three batches of XPA Tablets

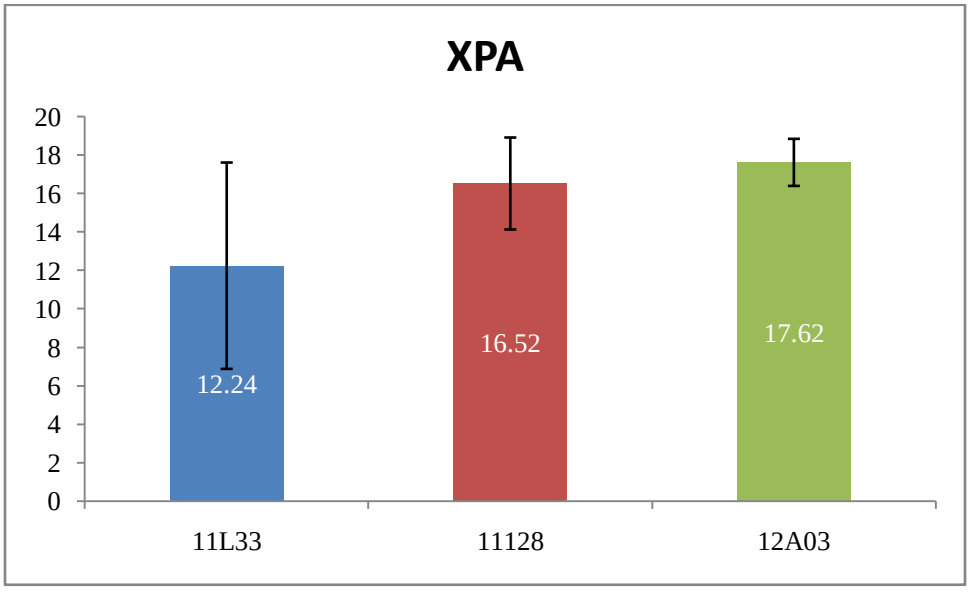


Table 27: Hardness test of 3 batches of SERVIGESIC Tablet

Brand Name	Tab No	Hardness (kg)		
		Batch no# 1998	Batch no# 8914	Batch no# 2017
SERVIGESIC	1	12.3	8.6	9.1
	2	7.6	6.7	9.7
	3	9.9	6.5	8.9
	4	6.1	6.4	15.2
	5	6.9	6.9	16.9
	6	10.9	7.1	14.9
	7	9.7	7.9	7.4
	8	9.9	7.5	14.0
	9	11.3	12.6	7.4
	10	9.6	7.2	16.4

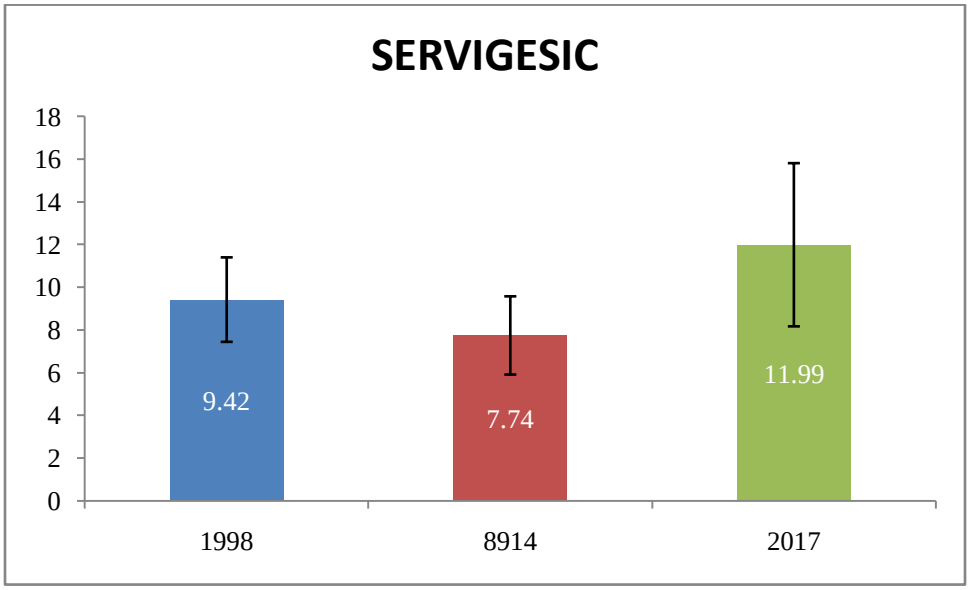
The hardness of the tablets ranged from 6.1 to 12.3kg in Batch No-1998, 6.4 to 12.6kg in Batch No-8914 and 7.4 to 16.9kg in Batch No-2017.

Table 28: Mean hardness and standard deviation of hardness of the three batches of SERVIGESIC Tablets

Brand	Batch	Mean weight (g)	Standard deviation
SERVIGESIC	1998	9.42	1.979
	8914	7.74	1.833
	2017	11.99	3.824

The mean hardness and standard deviation of three batches of SERVIGESIC tablets. Batch No- 1998 has mean value 9.42 and standard deviation 1.979. Batch No- 8914 has mean value 7.74 and standard deviation 1.833. Batch No- 2017 has mean value 11.99 and standard deviation 3.824

Figure 20: Mean hardness and standard deviation of the three batches of SERVIGESIC Tablets



7.1Friability test:

Table 29: Percentage friability of ACE Tablet

Brand	Batch	Initial weight of 10 tablets	Final weight of 10 tablets	% friability
ACE	1100304	5.75	5.70	0.87
	1100274	5.71	5.68	0.53
	1110202	5.78	5.75	0.52

The percentage friability of Batch# 1100304 was 0.87%, Batch# 1100274 was 0.53% and Batch# 1110202 was 0.52%.

Table 30: Percentage friability of FAST Tablet

Brand	Batch	Initial weight of 10 tablets	Final weight of 10 tablets	% friability
FAST	XC1099	6.36	6.35	0.16
	XC1021	6.37	6.36	0.16
	XC1076	0.65	0.64	1.56

The percentage friability of Batch# XC1099 was 0.16%, Batch# XC1021 was 0.16% and Batch# XC1076 was 1.56%.

Table 31: Percentage friability of XCEL Tablet

Brand	Batch	Initial weight of 10 tablets	Final weight of 10 tablets	% friability
XCEL	LE31	6.21	6.20	0.16
	KE125	6.25	6.24	0.16
	OE136	6.05	6.04	0.17

Table 28 showing the percentage friability of Batch# LE31 was 0.16%, Batch# KE125 was 0.16% and Batch# OE136 was 0.17%.

Table 32: Percentage friability of XPA Tablet

Brand	Batch	Initial weight of 10 tablets	Final weight of 10 tablets	% friability
XPA	11L33	6.00	5.96	0.67
	11128	5.96	5.95	0.17
	12A03	5.95	5.94	0.17

Table 29 showing the percentage friability of Batch# 11L33 was 0.67%, Batch# 11128was 0.17% and Batch# 12A03 was 0.17%.

Table 33: Percentage friability of SERVIGESIC Tablet

Brand	Batch	Initial weight of 10 tablets	Final weight of 10 tablets	% friability
SERVIGESIC	1998	6.02	6.00	0.33
	8914	5.95	5.94	0.17
	2017	6.04	6.03	0.17

The percentage friability of Batch# 1998 was 0.33%, Batch# 8914 was 0.17 and Batch# 2017 was 0.17%.

8.1 Disintegration test:

Table 34: Disintegration time of ACE Tablet

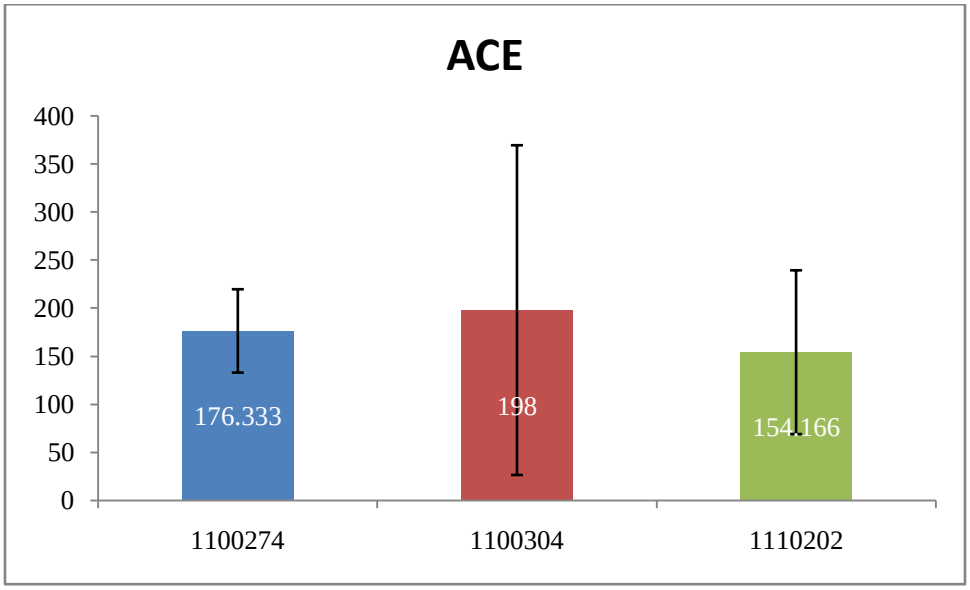
	Tab No	Disintegration (sec)		
		Batch no# 1100274	Batch no# 1100304	Batch no# 1110202
ACE	1	130 sec	49 sec	62 sec
	2	135 sec	86 sec	77 sec
	3	155 sec	106 sec	92 sec
	4	189 sec	129 sec	220 sec
	5	212 sec	337 sec	235 sec
	6	237 sec	481 sec	239 sec

In Batch No-1100274, the obtained disintegration time is 2 min 10 sec – 3 min 57 sec, in Batch No- 1100304 the obtained disintegration time is 49 sec-8 min 1 sec, In Batch No-1110202 the obtained disintegration time is 1 min 2 sec – 3 min 59 sec.

Table 35: Mean value and standard deviation of disintegration time of the three batches of ACE Tablets

Brand	Batch	Mean weight (g)	Standard deviation
ACE	1100274	176.333	43.412
	1100304	198	171.685
	1110202	154.166	85.298

Figure 21: Mean and standard deviation of the disintegration time of three batches of ACE Tablets



The mean and standard deviation of disintegration time of three batches of ACE tablets. Batch No-1100274 has mean value 176.333 and standard deviation 43.412. Batch No- 1100304 has mean value 198 and standard deviation 171.685. Batch No- 1110201 has mean value 154.166 and standard deviation 85.298.

Table 36: Disintegration time of FAST Tablets

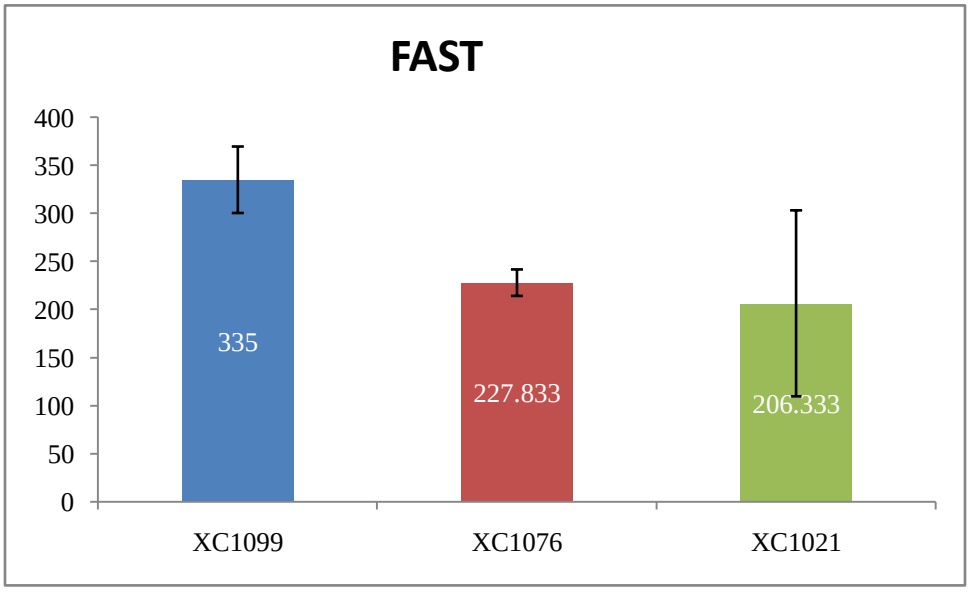
		Disintegration (sec)		
	Tab No	Batch no# XC1099	Batch no# XC1076	Batch no# XC1021
FAST	1	278 sec	209 sec	124 sec
	2	321 sec	212 sec	164 sec
	3	329 sec	232 sec	178 sec
	4	342 sec	235 sec	184 sec
	5	368 sec	238 sec	190 sec
	6	372 sec	241 sec	398 sec

In Batch No-XC1099, the obtained disintegration time is 4 min 38 sec -6 min 12 sec, in Batch No- XC1076 the obtained disintegration time is 3 min 29 sec – 4 min 1 sec, In Batch No-XC1021 the obtained disintegration time is 2 min 4 sec – 6 min 38 sec.

Table 37: Mean value and standard deviation of disintegration time of the three batches of FAST Tablets

Brand	Batch	Mean weight (g)	Standard deviation
FAST	XC1099	335	34.606
	XC1076	227.833	13.790
	XC1021	206.333	96.824

Figure 22: Mean and standard deviation of the disintegration time of three batches of FAST Tablets



The mean and standard deviation of the disintegration time of three batches of FAST tablets. Batch No- XC1099 has mean value 335 and standard deviation 34.606. Batch No- XC1076 has mean value 227.833 and standard deviation 13.790. Batch No- XC1021 has mean value 206.333 and standard deviation 96.824.

Table 38: Disintegration time of XCEL Tablets

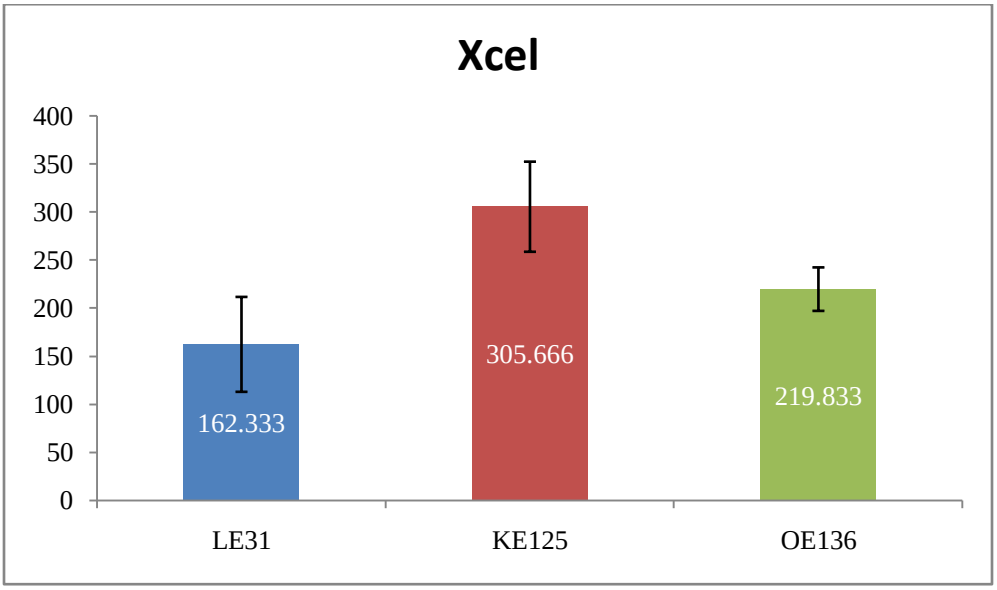
	Tab No	Disintegration (sec)		
		Batch no# LE31	Batch no# KE125	Batch no# OE136
XCEL	1	98 sec	259 sec	189 sec
	2	110 sec	272 sec	209 sec
	3	166 sec	283 sec	217 sec
	4	176 sec	311 sec	221 sec
	5	202 sec	320sec	225 sec
	6	222 sec	389 sec	258 sec

In Batch No-KE125, the obtained disintegration time is 4 min 19 sec – 6 min 29 sec, in Batch No- OE136 the obtained disintegration time is 3 min 9 sec – 4 min 18 sec. In Batch No-LE31 the obtained disintegration time is 1 min 38 sec – 3 min 42 sec.

Table 39: Mean value and standard deviation of disintegration time of the three batches of XCEL Tablets

Brand	Batch	Mean weight (g)	Standard deviation
OE136	LE31	162.333	49.419
	KE125	305.666	46.911
	OE136	219.833	22.631

Figure 23: Mean and standard deviation of the disintegration time of three batches of XCEL Tablets



The mean and standard deviation of the disintegration time of three batches of XCEL tablets. Batch No- LE31 has mean value 162.333 and standard deviation 49.419. Batch No- KE125 has mean value 305.666 and standard deviation 46.911 Batch No- OE136 has mean value 219.833 and standard deviation 22.631.

Table 40: Disintegration time of XPA Tablets

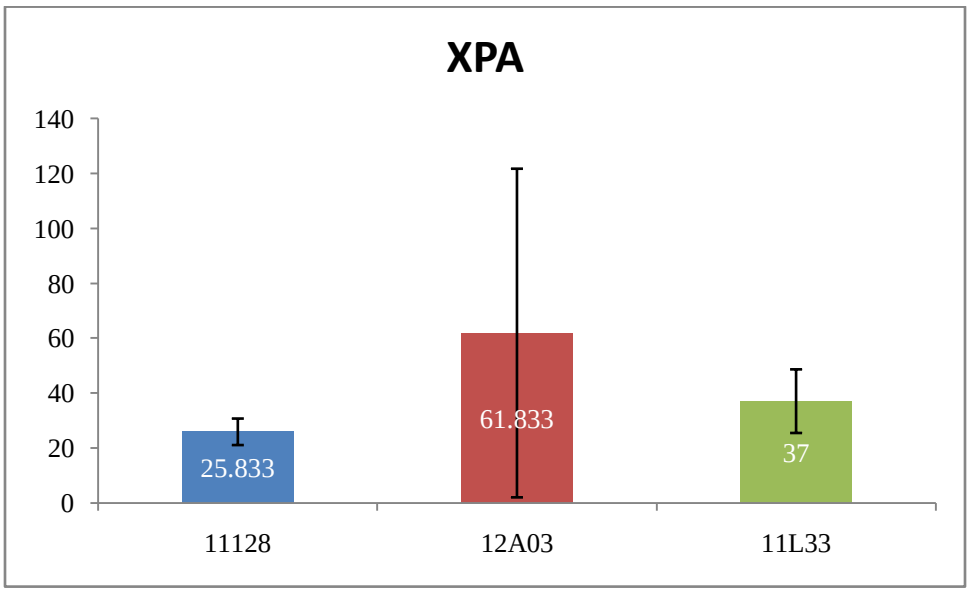
		Disintegration (sec)		
	Tab No	Batch no# 11128	Batch no# 12A03	Batch no# 11L33
XPA	1	20 sec	30 sec	28 sec
	2	22 sec	32 sec	31 sec
	3	23 sec	34 sec	33 sec
	4	28 sec	40 sec	34 sec
	5	30 sec	52 sec	36 sec
	6	32 sec	183 sec	60 sec

In Batch No-11128, the obtained disintegration time is 20sec-32sec, in Batch No- 12A03 the obtained disintegration time is 30 sec-3 min 3 sec, In Batch No-11L33 the obtained disintegration time is 28 sec-1min.

Table 41: Mean value and standard deviation of disintegration time of the three batches of XPA Tablets

Brand	Batch	Mean weight (g)	Standard deviation
XPA	11128	25.833	4.833
	12A03	61.833	59.887
	11L33	37	11.593

Figure 24: Mean and standard deviation of the disintegration time of three batches of XPA Tablets



The mean and standard deviation of the disintegration time of three batches of XPA tablets. Batch No- 11128 has mean value 25.833 and standard deviation 4.833. Batch No- 12A03 has mean value 61.833 and standard deviation 59.887. Batch No- 11L33 has mean value 37 and standard deviation 11.593.

Table 42: Disintegration time of SERVIGESIC Tablet

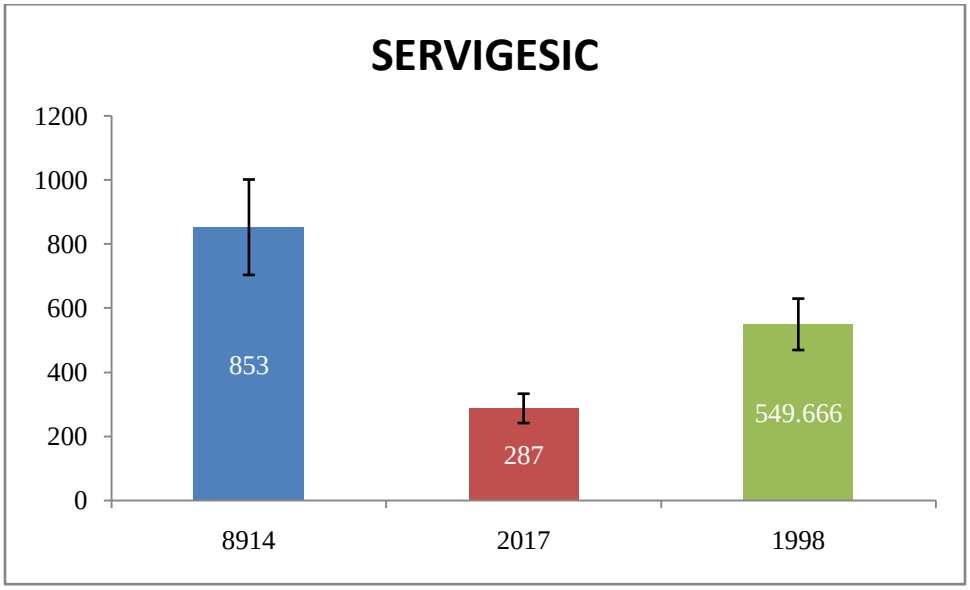
	Tab No	Disintegration (sec)		
		Batch no# 8914	Batch no# 2017	Batch no# 1998
SERVIGESIC	1	586 sec	228 sec	424 sec
	2	838 sec	255 sec	504 sec
	3	846 sec	281 sec	550 sec
	4	888 sec	293 sec	576 sec
	5	925 sec	304 sec	582 sec
	6	1035 sec	362 sec	662 sec

In Batch No-8914, the obtained disintegration time is 9 min -17 min 15 sec, in Batch No- 2017 the obtained disintegration time is 3 min 48 sec – 6 min 02 sec, In Batch No-1998 the obtained disintegration time is 7 min 4 sec-11 min 2 sec.

Table 43: Mean value and standard deviation of disintegration time of the three batches of SERVIGESIC Tablets

Brand	Batch	Mean weight (g)	Standard deviation
SERVIGESIC	8914	853	149.061
	2017	287.166	45.805
	1998	549.666	80.293

Figure 25: Mean and standard deviation of the disintegration time of three batches of SERVIGESIC Tablets



The mean and standard deviation of the disintegration time of three batches of SERVIGESIC tablets. Batch No- 8914 has mean value 853 and standard deviation 149.061. Batch No- 2017 has mean value 287.166 and standard deviation 45.805. Batch No- 1998 has mean value 549.666 and standard deviation 80.293.

Chapter -5
Discussion

9.1 Discussion:

9.1.1: Weight Variation test:

In this research work Shimdzu AY220 analytical balance was used to measure the weight of different batches of different brands of paracetamol tablets and calculation done carefully. Surprisingly % weight variation of all tablets was within acceptable range.

In case of the weight variation of three different batches of ACE tablet no tablets exceed the ± 5 % variation. That means the three batches of ACE tablets (1100304, 1100274 and 1110202) comply with the specification mentioned in the USP and pass the quality control parameter. The weight variation of three different batches of FAST tablet also did not exceed the ± 5 % variation. That means the three batches of FAST tablets (XC1099, XC1021 and XC1076) also comply with the specification mentioned in the USP and pass the quality control parameter. The weight variation of three different batches of XCEL tablet did not exceed the ± 5 % variation. That means the three batches of XCEL tablets (LE31, KE125 and OE136) comply with the specification mentioned in the USP and pass the quality control parameter. The weight variation of two batches of XPA tablet exceeds the ± 5 % variation. Batch 11L33 comply with the USP specification but batch 11128 and batch 12A03 do not comply with the USP specification. In batch 11128 the average weight of XPA found 0.60g and the % weight variation ranged from -1.64 to 7.41%. Since more than two tablets are outside the range of ± 5 %, the tablets do not comply with the specification. In batch 12A03 the average weight of XPA found 0.60g and the % weight variation ranged from 1.69 to 15.38%. Since more than two tablets are outside the range of ± 5 %, the tablets do not comply with the specification. The weight variation of three different batches of SERVIGESIC tablet did not exceed the ± 5 % variation. That means the three batches of SERVIGESIC tablets (2017, 1998 and 8914) comply with the specification

mentioned in the USP and pass the quality control parameter. The tablets those meet weight variation specification ensure good content uniformity and those do not meet the specification indicate that the content uniformity is poor.

9.1.2: Hardness test:

The Hardness test is performed to measure the degree of force required to break a tablet. In this study VEEGO hardness tester is used to measure the hardness of 150 tablets of different batches of different brands of Paracetamol. All measured values meet the specification. USP specifies that hardness of any tablets must not be lower than 4 kg. All three batches of ACE (1100304, 1100274 and 1110202), FAST (XC1099, XC1021 and XC1076), XCEL (LE31, KE125 and OE136), XPA (11L33, 11128 and 12A03) and SERVIGESIC (1998, 8914 and 2017) have a hardness greater than 4kg and, therefore, meet the USP specification and pass the quality control parameter.

9.1.3: Friability test:

USP specifies that if friability study is performed with ten tablets of any batch they must not lose 1% of their initial weight. All three batches of ACE (1100304, 1100274 and 1110203), FAST (XC1099, XC1021), XCEL (LE31, KE125 and OE136), XPA (11L33, 11128 and 12A03) and SERVIGESIC (1998, 8914 and 2017) have meet the USP specification and passed the friability test . But XC1076 batch of FAST brand does not meet the USP specification since the % friability of this batch found 1.56%.

9.1.3: Disintegration test:

Disintegration test is very imperative since disintegration time is one of the most important physical parameter of solid dosage form. It related with the bioavailability. In this research the disintegration time of each tablets was observed carefully in prepared acidic medium. According

to USP uncoated tablets have disintegration time standard as low as 5 min but the majority of the tablets have a maximum disintegration time 30 min. All three batches of ACE tablets (1100304 ,1100274, 1110202), FAST (XC1099, XC1021 and XC1076), XCEL (LE31, KE125 and OE136), XPA (11L33, 11128 and 12A03) and SERVIGESIC (1998, 8914 and 2017) have meet the USP specification and passed the disintegration test .

Chapter -6
Conclusion

10.1 Conclusion:

Paracetamol is a well established and verified analgesic and antipyretic drug which has an admirable safety profile when taken at recommended dose. The current pharma market of Bangladesh is inundated with different brands of paracetamol and the quality control test is imperative to monitor these approved brands in order to adequately assess the quality, therapeutic effectiveness and safety profile of Paracetamol. According to my knowledge, so far only one study is conducted by Karmakar, & Kibria, 2012, to compare the quality control parameters between paracetamol and paracetamol/caffeine tablets. Since no further study was conducted regarding this topic so this research work was selected. In this study it was observed that all the batches complied with the BP and USP specification except two batch of XPA (batch 11128 & 12A03) which did not meet the percentage of weight variation test and one batch of FAST (batch XC1076) also did not meet the percentage of friability test. However, very little variation was observed among different brands and this pharmaceutical equivalence lend a hand to conclude that any of these five brands can be used.

Chapter -7
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