Napata College

Faculty of Pharmacy

Batch (2)

Comparative in Vitro Quality Evaluation of Two Brands Of Folic Acid 5mg Tablets available at Sudan markets

A thesis submitted by the faculty of pharmacy of Napata college in partial fulfillment of the requirements of B.S.c. degree in pharmacy

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بسم الله الرحمن الرحيم

الآية

قَالَ تَعَالَىٰ: ﴿ وَمَآ أَرۡسَلۡنَا مِن قَبۡلِكَ إِلَّا رِجَالٗا نُّوحِيٓ إِلَيۡهِمۡۚ فَسۡـَٔلُوٓاْ أَهۡلَ ٱلذِّكۡرِ إِن كُنتُمۡ لَا تَعۡلَمُونَ ٤٣ ﴾

صدق الله العظيم

سورة النحل: ٤٣

Dedication

To my dear parents ,my god protect them.

To all the generous family that has supported me ,my brothers and sisters .

To all the doctors of department of pharmacy at Napata college.

TO my companions who shared my best moments with me.

To all may colleagues in batch second .

To all those who had a beautiful impact in my life , and to all those whom my loved and forgot pen……

I dedicate to you the fruits of this humble effort ….

Thank you ….

Acknowledgment

First ,we thank God for everything and for enabling us to present this project in the best way we wanted. We would like to thank our supervisor for this project Dr.Randa Abdulatif , for coming up with this project . We thank the faculty and clinicians who have given us all the knowledge. Most of all we are all grateful to our families for their endless love , help , support and encouragement , thank you for continuous giving. And to our friends for understanding and support for us to complete this project , and we hope that it will have a role in helping the community.

الحمد لله وكفى والصلاة والسلام على الحبيب المصطفي وأهله ومن وفىّ اما بعد : الشكر لله أولاً واخيراً الذي وفقنا لتثمين هذه الخطوة في مسيرتنا الدراسية و إتمام هذا المشروع بأفضل شكل أردناه ، ولأنه من لا يشكر الناس لا يشكر الله نود أن نقدم الشكر لمشرفنا علي هذا البحث دكتوره رنده عبداللطيف لمساعدتنا بالخروج بهذا البحث ، والشكر مقدم لأعضاء هيئة التدريس و للدكاترة الذين قدموا لنا كل الجهود من اجل العلم و المعرفة . جميعنا ممتنون لعائلاتنا علي حبهم ومساعدتهم ودعمهم وتشجيعهم الذي لا نهاية له شكراً كثيراً لكم علي عطائكم المستمر. شكرا لأصدقائنا لمساندتهم ودعمهم الدائم لإكمال هذا المشروع و نتمني ان يكون له دوراً في مساعدة المجتمع

شكرا للجميع.....

Abstract

Folic acid is the synthetic version of the vitamin folate, also known as vitamin B9.

The purpose of this study was to evaluate the pharmaceutical quality of the Folic acid tablets dispensed in sudan. Two different brands of immediate release Folic acid tablets were tested for weight variation , hardness, friability, disintegration time, and dissolution. The result showed all marketed products comply with established limit.

Keywords:

Folic acid tablet, In-vitro quality, weight variation, friability, disintegration, Hardness, dissolution .

ملخص البحث

حمض الفوليك هو النسخة الاصطناعية من فيتامين ب 9. الغرض من هذه الدراسة هو تقييم الجودة الصيدلانية لأقراص حمض الفوليك الموزعة في السودان. تم اختبار علامتين تجاريتين مختلفتين من أقراص حمض الفوليك ذات الإطلاق الفوري من أجل اختلاف الوزن والصلابة والتفتت ووقت التفكك والذوبان. أظهرت النتيجة أن جميع المنتجات المسوقة تتوافق مع الحدود الموضوعة

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List of Abbreviations

Abbreviations	Meaning
API	Active Pharmaceutical Ingredient
SL	Sublingual
SR	Sustained Release
QC	Quality Control
LP	Local Production
LMIC	Low and Middle Income Countries
DHF	Dihydro Floate
THF	Tetra Hydro Folate
DHFR	Dihdro Folate Reductase
NHANES	National Health and Nutrition Examination Survey
NADPH	Nicotinamid Adenine Dinucleotide Phosphate Hydrogen
NTP	National Toxicology Program
MTHFR	Methyl Tetrahydro Folate Reductase
DUMP	Deoxyuridine Monophosphate
DTMP	Deoxthymidine Monophosphate
USA	United States of America
DNA	Deoxyribonucleic Acid
RBC	Red Blood Cell
U.S	United States
RNA	Ribonucleic Acid

CHAPTER ONE

Introduction ,Study Justification ,literature Review and Objective

1. Introduction

Pharmaceutical dosage forms pharmaceutics is science of dosage form design. pharmaceutical dosage forms are consisted of active drug substance (active pharmaceutical ingredient) and excipients. active drug substances (active pharmaceutical ingredients, API) are chemical compounds with pharmacological intended for use in diagnosis, treatment or prophylaxis of disease[1].Excipients or additives are inactive pharmaceutical ingredients including diluents/fillers, binders, lubricants, coatings, preservatives, colorants, flavoring agents and disintegrants، direct clinical use of the active drug substances " as they are" is rare due to the number of good reasons[1].

API handling can be difficult or impossible (e.g., low mg and µg doses)، accurate drug dosing can be difficult or impossible ، API administration can be impractical, unfeasible or not according to the therapeutically aims، some API can benefit from reducing the exposure to the environmental factors (light, moisture), or they need to be chemically stabilized due to the inherent chemical instability ، API can be degraded at the site of administration (e.g., low pH in stomach) ، API may cause local irritations or injury when they are present at high concentrations at the site of administration ، and API can have unpleasant organoleptic qualities (taste, smell) .[1]

Solid dosage forms are the most important dosage forms for pharmaceuticals, which contain a unit dose of one or more drugs. Commonly used solid dosage forms are powders, granules, tablets, capsules, etc., accounting for about 70% of the pharmaceutical preparations. Compared with liquid dosage forms, solid dosage forms have good physical and chemical stability, lower manufacturing costs, and are easy to take and carry, the pretreatment of the preparation process undergoes the same unit operation to ensure uniform mixing and accurate dosage of the drug, and there is a close relationship between the dosage forms. [2]

Tablets are solid dose pharmaceutical preparation containing drug substances 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. It has been estimated that solid-dosage forms constitute approximately 90% of all dosage forms clinically used to provide systemic administration of therapeutic agents. The

widespread use of tablets has been achieved as a result of their convenience and also the diversity of tablet types.[3]

Tablets are prepared primarily by compression of granules or powder blends, with a limited number prepared by moulding. Most tablets are used in the oral administration of drugs. Many of these are prepared with colourants and coatings of various types. Other tablets, such as sublingual, buccal, or vaginal tablets, are prepared to have features most applicable to their particular route of administration. [3]

General Properties of Tablets A tablet must be strong and hard to withstand mechanical shock during manufacturing, packing, shipping, dispensing and use. The drug content of the tablet must be bioavailable that is, the tablet must be able to release its content in a predictable and reproducible manner. The tablet must be chemically and physically stable to maintain its chemical and physical attributes during manufacture, storage, and use. The tablet should have elegant product identity which is free from any tablet defect. Tablets must be uniform in weight and in drug content. [3]

Sublingual (S.L) and buccal Tab Buccal and sublingual tablets intended to be dissolved in the buccal pouch (buccal tablets) or beneath the tongue (sublingual tablets) for absorption through the oral mucosa. Drugs used by this route are for quick systematic action. They enable oral absorption of drugs that are destroyed by the gastric juice and/or are poorly absorbed from the gastrointestinal tract. Buccal tablets are designed to erode slowly, whereas those for sublingual use (such as nitroglycerin) dissolve promptly and provide rapid drug effects. [4]

Chewable Tab These are intended to be chewed in the mouth before swallowing. These have a creamy base, usually of specially flavored and colored mannitol Chewable tablets are especially useful for administration of large tablets to children and adults who have difficulty swallowing solid dosage forms. [4]

Effervescent Tab Effervescent tablets are prepared by compressing granular effervescent salts (active ingredient with mixture of organic acid such as citric acid or tartaric acid and sodium bicarbonate) that release gas when in contact with water. These tablets generally contain medicinal substances that dissolve rapidly when added to water and produce a solution rapidly with the release of carbon dioxide. The ―bubble action‖ can assist in breaking up the tablets and enhancing the dissolution of the active drug [4].

Sustained release (S.R.)Tab or Retard Tab Time release technology (also known as sustained release, extended release, controlled release, retard and other synonyms) is a mechanism used in tablets to dissolve a drug over time in order to be released slower and steadier into the bloodstream while having the advantage of being taken at less frequent intervals than immediate-release formulations of the same drug. [4]

Scored and Double scored Tab Tablets that can be broken in half or quarters will be scored by the manufacturer to make the process easier[4]

Advantages of Tablets in the Pharmaceutical industry Tablets are elegant in appearance and convenient to use They are superior to other dosage forms with respect to chemical, physical and microbiological stability Tablets provide stable and an accurately measured dosage of drug substance to patients. Tablets can be formulated to protect unstable drug substances or disguise unpalatable excipients tablets are generally inexpensive to manufacture. It is easier to mask the unpleasant taste of some APIs in tablets thus improving patient acceptability. Tablets may be formulated to contain two or more drug substances (even if they are physically or chemically incompatible), thus reducing multiple tablet use[4].

Tablets may be easily manufactured to show product identification using coloured coatings, embossed markings, and printing. Tablets may be designed to release their active substance at a particular site within the gastrointestinal tract to reduce side effects, promote absorption at that site or provide a local effect (e.g. ulcerative colitis).With the exception of proteins which are denatured in the gastrointestinal tract, all classes of therapeutic agents may be administered orally in the form of tablets . [4]

Disadvantages of Tablets The manufacture of tablets requires a series of unit operations (weighing, milling, drying, mixing etc.) thus there is an increased level of product loss at each stage in the formulation process. The absorption of medicament from tablets is dependent on physiological factors, such as gastric resident/emptying time, and thus, vary from one .patient to another. The compression properties of certain drug substance are poor and may present problems in their subsequent formulation and manufacture as tablets. [4]

Immediate release tablets are those which disintegrate rapidly and get dissolved to release the medicaments Immediate release may be provided for by way of an appropriate pharmaceutically acceptable diluent or carrier, which diluent or carrier

does not prolong, to an appreciable extent, the rate of drug release and/or absorption . [5]

Bioequivalence studies are very important for the development of a pharmaceutical preparation in the pharmaceutical industry. Their rationale is the monitoring of pharmacokinetic and pharmacodynamics parameters after the administration of tested drugs. The target of such study is to evaluate the therapeutic compatibility of tested drugs (pharmaceutical equivalents or pharmaceutical alternatives). The importance of bioequivalence studies is increasing also due to the large growth of the production and consumption of generic products. Generic products represent approximately 50 % of the whole consumption in many European countries and USA. [6]

The search output of bioequivalence study is together with the pharmaceutical quality data of medical product one of the main part of the registration file submitted to a national regulatory authorities .the registration of generic products does not demand complicated and expensive clinical study contrary to original product. The complicated and expensive clinical study contrary to original product .The comparison of the original and the generic product via bioequivalence study is suggested as sufficient. the aim of this article is to provide to a medical public a summary about the types of bioequivalence studies ,their range, rules of their practice and let them gain their own attitude to this question .[6]

Quality Control (QC) is a system of routine technical activities, to measure and control the quality of the inventory as it is being developed. The QC system is designed to Provide routine and consistent checks to ensure data integrity, correctness and completeness ، Identify and address errors and omissions ، also Document and archive inventory material and record all QC activities . [7]

QC activities include general methods such as accuracy checks on data acquisition and calculations and the use of approved standardized procedures for emission calculation ,measurements ,estimating uncertainties ,archiving information and reporting .Higher tier QC activities include technical reviews of source categories ,activity and emission factor data ,and methods. [7]

Local production (LP) of essential medical technologies is at the interface of industrial/economic development policy and public health policy. From an industrial policy perspective, generating assured quality products by having a competitive

pharmaceutical/ medical device industry with sufficient economies of scale would be desirable for low and middle income countries (LMICs) .[8]

The drug in this study will be folic acid 5 mg tablet.

2. Literature Review

Folate is water _soluble B vitamin that is involved in nucleotide biosynthesis, the methionine cycle ,serine and glycine biosynthesis, and biological methylation reactions. [9,10]

Folic acid is a water-soluble B-complex vitamin found in foods such as liver, kidney, yeast, and leafy, green vegetables. Also known as folate or Vitamin B9, folic acid is an essential cofactor for enzymes involved in DNA and RNA synthesis. More specifically, folic acid is required by the body for the synthesis of purines, pyrimidines, and methionine before incorporation into DNA or protein. Folic acid is the precursor of tetrahydrofolic acid, which is involved as a cofactor for transformylation reactions in the biosynthesis of purines and thymidylates of nucleic acids. [11,12]

Impairment of thymidylate synthesis in patients with folic acid deficiency is thought to account for the defective deoxyribonucleic acid (DNA) synthesis that leads to megaloblast formation and megaloblastic and macrocytic anemias. Folic acid is particularly important during phases of rapid cell division, such as infancy, pregnancy, and erythropoiesis, and plays a protective factor in the development of cancer. As humans are unable to synthesize folic acid endogenously, diet and supplementation is necessary to prevent deficiencies. In order to function properly within the body, folic acid must first be reduced by the enzyme dihydrofolate reductase (DHFR) into the cofactors dihydrofolate (DHF) and tetrahydrofolate (THF). [11,12]

This important pathway, which is required for de novo synthesis of nucleic acids and amino acids, is disrupted by anti-metabolite therapies such as [DB00563] as they function as DHFR inhibitors to prevent DNA synthesis in rapidly dividing cells, and therefore prevent the formation of DHF and THF. In general, folate serum levels below 5 ng/mL indicate folate deficiency, and levels below 2 ng/mL usually result in megaloblastic anemia. [11,12]

Origin of the substance [13,14,15]

Synthetic folic acid is commercially available.

Chemical names N-[4(2-Amino-4-hydroxypteridin –6- ylmethylamino) benzoyl]-L(+)-glutamicacid.N-{4-[[(2-Amino-1,4-dihihydro-4-oxo-6-pteridinyl) methyl] amino] benzoyl}-L-glutamicacid.N-{p-[[2-amino-4hydroxy-6-pteridinyl) methyl]amino]benzoyl}-L-glutamic acid .

Molecular formula C19H19O6

Molecular weight 441.4

Colour Yellow to orange brown

State/Form Crystalline powder

Description Odorless

Solubility Readily soluble in alkali, hydroxides and carbonates. Insoluble in alcohol, acetone, chloroform and ether. Solutions are inactivated by ultraviolet light. Alkaline solutions are sensitive to oxidation and acid solutions are sensitive to heat.

pKa 4.7,6.8,9.0 (30°) . Dissociation constant.

Shelf-life of the substance No data available.

Biomarkers of folate status Folate status can be determined by serum and RBC folate concenterations as well as homocysteine concentrations Serum folate concentrations reflect short-term dietary intake and RBC folate concentrations reflect long-term status and is considered more reflective of folate tissue stores . RBC folate is directly reflective of bone marrow folate stores at the time of erythropoiesis and the 120-day turnover rate of RBC makes this measure resistant to short-term folate variation . RBC folate concentrations are used to diagnose clinical folate deficiency. [16]

According to WHO standards, RBC folate concentrations of <340 nM or serum folate concentrations of <10 nM observed repeatedly over a 1-month period are indicative of folate deficiency . There are currently no established high cut-offs for RBC and serum folate concentrations. The 97th percentile of RBC folate concentrations (1360 nM) National Health and Nutrition Examination Survey (NHANES) has been used as an arbitrary cut- off by Colapinto et al. [16]

Homocysteine is a nonspecific inverse indicator of folate status and at concentrations above 16 µM can indicate folate deficiency but lower levels have been used . Folate, in the form of 5MTHF, is required to remethylate homocysteine to methionine.

During folate deficiency, there is reduced conversion of homocysteine to methionine, thereby increasing homocysteine concentrations . Raised homocysteine concentrations can also indicate inadequate vitamin B12 and vitamin B6 status . Renal dysfunction and aging can also raise homocysteine concentrations . [16]

Folic acid is used for preventing and treating low blood levels of folate (folate deficiency) and high blood levels of homocysteine (hyperhomocysteinemia). People who are pregnant or might become pregnant take folic acid to prevent serious birth defects such as spina bifida. Folic acid is also used for many other conditions including depression, stroke, decline in memory and thinking skills, and many others. [17]

Mechanism of Action Folate is mainly concentrated in the liver.[18] The synthetic form, folic acid, is given as dihydrofolate (DHF) and is converted to THF by the action of the dihydrofolate reductase enzyme, which depends on nicotinamide adenine dinucleotide phosphate hydrogen (NADPH). THF then converts to 5-10-methylenetetrahydrofolate (5-10-MTHF), which can diverge down different paths: toward DNA synthesis via dTMP or toward methionine synthesis.[19]

For DNA synthesis, deoxyuridine monophosphate (dUMP) accepts one methyl group from 5-10-MTHF—via thymidylate synthase, which accepts the other—to become deoxythymidine monophosphate (dTMP) and allows the cell cycle to continue while simultaneously regenerating DHF. Drugs used in cancer chemotherapy disrupt this process by inhibiting vital enzymes necessary for cell cycle progression. Methotrexate, for example, inhibits dihydrofolate reductase. By reducing available THF and its downstream components, methotrexate indirectly deprives thymidylate synthase of its substrates.[20]

Methionine is a byproduct synthesized as folate reduces homocysteine levels in the blood; 5-10-MTHF donates a methyl group to an enzyme, methyl-tetrahydrofolate reductase (MTHFR), and then becomes 5-methyl THF.[20] 5-methyl THF donates its remaining methyl group to homocysteine via methionine synthase, converting homocysteine to methionine. This transfer of both methyl groups from the original 5-10-MTHF regenerates THF and re-enters the cycle. Vitamin B12 is a crucial cofactor for methionine synthase, and B12 deficiency can lead to macrocytic megaloblastic anemia, similar to that of folate deficiency but with additional clinical symptoms beyond the scope of this article.[21]

Adverse Effects For the general population, a diet that contains a daily amount of folic acid below the established upper intake level of 1000 mcg has not been demonstrated to result conclusively in any adverse health outcomes. The U.S. National Toxicology Program (NTP) examined areas of previous concern, including cognition (relating to vitamin B12 deficiency), cancer, diabetes- and thyroid-related disorders, and hypersensitivity-related outcomes. .[22,23]

that, for the areas considered, no definitive evidence exists for adverse effects due to folic acid.[22,23]

The chemical stability of folic acid in 25% dextrose, 3.5% amino acids, and multivitamin solution was investigated. Solutions of 0.25, 0.5, 0.75, and 1.0 mg/liter of folic acid admixed in the study solution were prepared. Solutions were stored in light-room temperature, light-refrigeration, dark-room temperature, or dark-refrigeration. Samples were drawn to determine initial folic acid concentration and again at 4, 8, 12, 18, 24, 36, and 48 hr after admixture.[24]

Folic acid concentration was determined by competitive binding radioassay, and results are expressed as percent of initial folic acid concentration. Folic acid was stable for 48 hr with each tested concentration and stability was found to be independent of temperature or light storage effects. Folic acid admixed in the study solution is chemically stable for up to 48 hr after initial admixture under normal total parenteral nutrition storage conditions.[24]

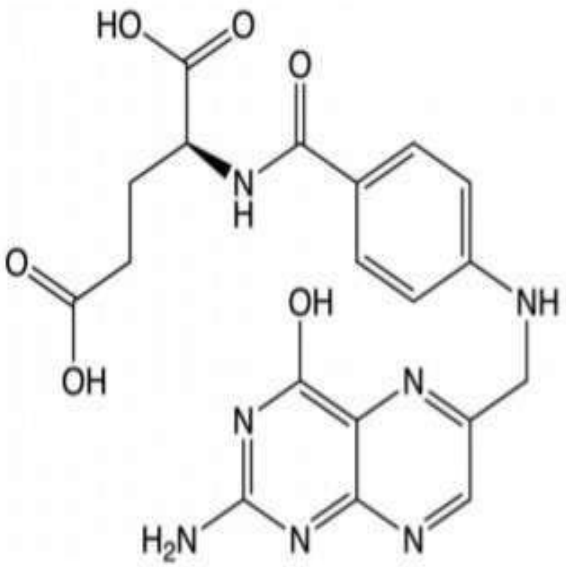

FIGURE 1 - Structure of the folic acid molecule.

3. Study Justification

The price of imported brands is the one of the big issues that affect indirectly the therapeutic effectiveness and some patient stopped taking drug because they cannot afford to pay them. If the result of this research indicated that no difference between imported and locally manufactured brands of folic acid tablets. This may a positive impact of the cost of such medication.Building consumer's trust for local medication is one of the main targets to achieve success in decreasing the need for the imported medications. While encouraging the local drug manufacturers.

4. Objective

General Objective

The objective of this study to compare the physiochemical and pharmaceutical property profile of two folic acid 5mg tablets commercially distributed in Sudan by which one is locally manufactured and other is an imported.

Specific Objective

The study was a single-blind comparative analysis of two brands of Folic acid 5mg tablets and this study intended .

- To evaluate the physical quality in their appearance, purity in their substance, friability on handling, and the content in their preparations .
- To evaluate the drug release using in-vitro dissolution test.
- To analyze the observations and make a comparison of the brands .

CHAPTER TWO

Material and method

5.Materials and Methods

6._ Two different brands of folic acid 5mg (local and imported).

_ Distilled water.

_ hydrochloric acid

Instruments

_ Analytical balance.

_ Disintegration tester (BIOBASE®).

_ Dissolution tester(BIOBASE®).

_ Hardness tester (BIOBASE®).

_ Friability tester (BIOBASE®).

_UV/Vis spectrophotometer(Leishangthem international®)

_Micrometer.

Study Design

Laboratory based comparative study.

Study Area

The drugs will be purchase from pharmacies in Khartoum state and experiments will be carried out in pharmaceutics and pharmaceutical chemistry lab of the Faculty Pharmacy in Napata College .

.Weight & weight variation

Twenty tablets from each brand was randomly selected and weighted individually and their average weight was calculated. percentage deviation from the average was calculated too**.** [25]

The test stated that different brands of Folic Acid tablets have passed the weight variation uniformity test as specified in the Indian Pharmacopoeia (not exceed ±10% deviation). [26]

Hardness test

The crushing strength of a tablet (hardness) was determined with a tablet hardness device. ten tablets was randomly selected from each brand and the pressure at which each tablet crush was recorded in kg/cm. [25]

It is important physical feature for assessing tablet. Different brands of Folic Acid tablets have acceptable crushing strength or hardness of more than 5kg/cm². [26]

Friability test

Twenty tablets was selected from each brand and weighted , and put into the friabilitor . Tablets were rotated at 25 rpm, for 4 minutes then weigh it again and the friability percentage was calculated for each batch**.** [25]

The friability value for different brands of Folic Acid tablets were ranged from 0.01-0.001%. In different brands of Folic Acid tablets formulation the percent (%) friability was less than 1% which ensure that all the tablets were mechanically stable. [26]

$$F = \frac{m_1 (100 - T_1) - m_2 (100 - T_2)}{m_1} \times 100$$

F = friability;

T_1= percentage loss on drying before the test (mean of 2 determinations);

T_2= percentage loss on drying after the test (mean of 2 determinations);

m_1= mass of the tablets before the test, in grams;

m_2=mass of the tablets after the test, in grams.

Disintegration test

This test was performed according to USP's methodology. Six samples of each formulation had to disintegrate in less than 30 minutes (USP 2014).

Disintegration is the process of breaking the tablet in to the small granules and it is prior step of drug dissolution and it is the part of In-vitro- In vivo correlation so the disintegration test determine the time required to breaking the tablet and pass all the particle from mesh size 10. USP disintegration apparatus (Elect lab ED-2L) containing six glass tubes will use for the purpose. [27]

one tablet of folic acid was placed in each tube and the basket rack is positioned in a 1 L beaker containing distilled at 37±2°C temperature. [27]

The instrument was operated with a motor driven device with 28-32 cycle/min frequency. When all the particles from all the six tubes passed from the tube mesh to the outer beaker that time was note as disintegration time after that the average time was note and this process was repeated for the two different brands of folic acid 5 mg tablets. [27]

Tables were satisfactory as uncoated IP tablets disintegration time standards as low as 15 min. the overall disintegration time for different brands of Folic Acid tablets brands was in the ranged from 1.08 – 2.44 min. [28]

Dissolution test

The tablet is placed within the basket positioned one inch above the bottom of the dissolution vessel and the vessel is held by a shaft that rotates and stirs the dissolution medium at 100 rpm. The 900 ml of 0.1 hydrochloric acid dissolution media was equilibrated to 37±1°C. In order to meet USP standards, 75% of the label amount of folic acid must be released out of the multivitamin unit in 60 minutes .[29]

Unlike the USP method, which gives a single point measurement, dissolution was followed for one hour and 0.5 ml from the dissolution medium from each vessel of the dissolution apparatus was withdrawn every 15 minutes and transferred to a common sampling receptacle. This allowed for the generation of a more complete dissolution profile. [29]

The assay was therefore performed on a pooled sample and provided an average of the folic acid release across the six dosage forms. The absorbance of filtrate was measured by UV spectrophotometer.[29]

Drug content

10 tablets were powdered and 100mg drug equivalent powder dissolved in suitable media buffer or 0.1N HCl. Volume of the solution made up to 100ml by that media. Solution was filtered and diluted 100times and analyzed spectrophotometric and further calculation carried out to determine drug content in one tablet . [30]

CHAPTER THREE

Results

7.Results

Table no (1): Weight Variation Test Of folic acid tablet brand

Brand	***SD%**
A	**7.50**
B	**8**

*SD: Standard deviation percentage

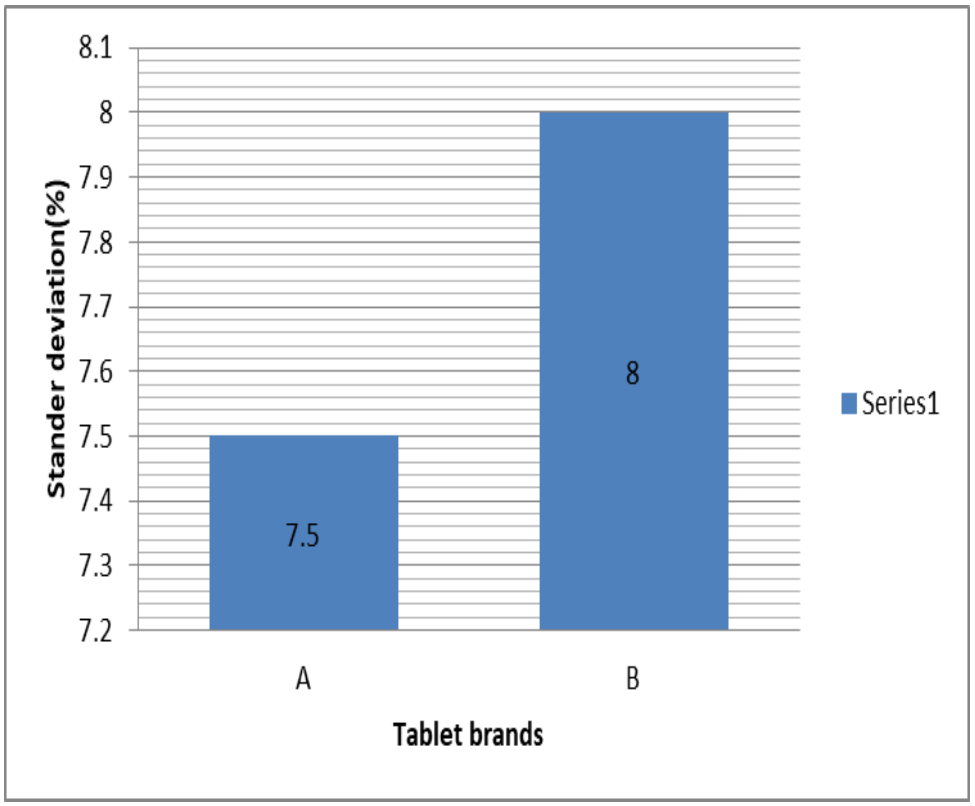

Figure no(2): weight variation test of folic acid tablet brands

Table no (2): Friability Test of folic acid tablet brand

Brand	**Friability %**
A	0.86
B	0.86

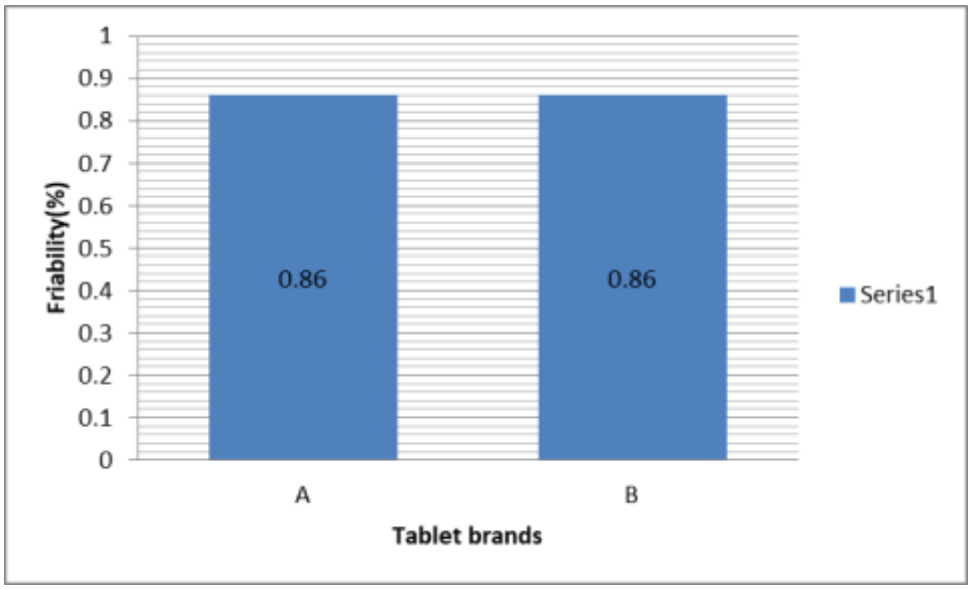

Figure no (3): friability test of folic acid tablet brands

Table no (3): Content Uniformity Test of folic acid tablet brand

Brand	**% of content**
A	102.4%
B	100.8%

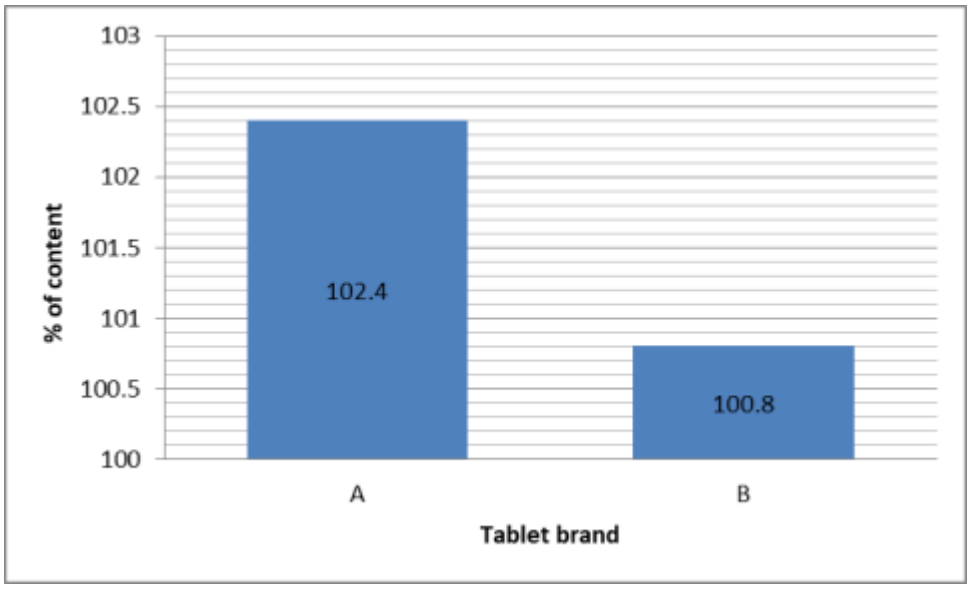

Figure no(4): Content Uniformity Test of folic acid tablet brands

Table no (4) :Disintegration Test of folic acid tablet brand

Brands	**Disintegration Time (Minute)**
A	1.5
B	0.5

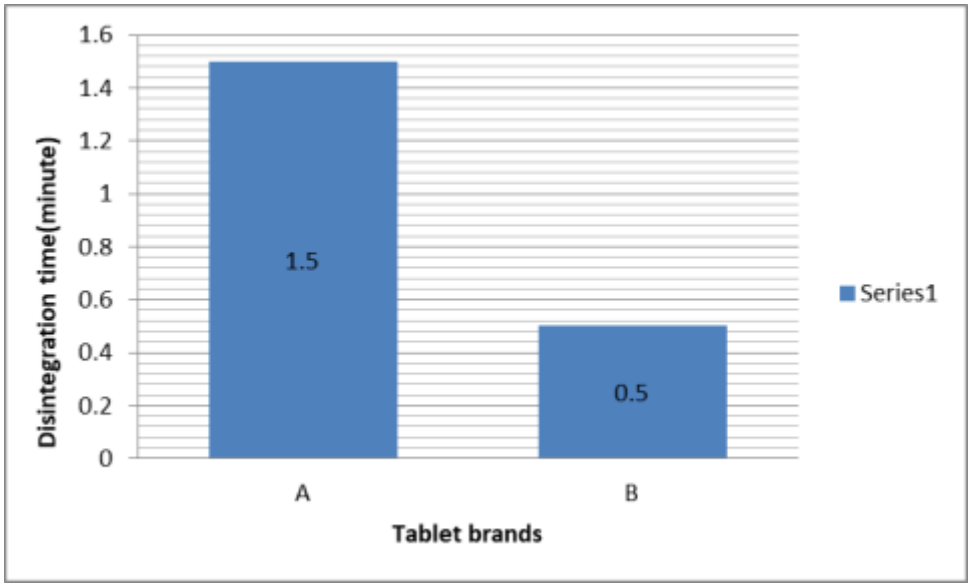

Figure no (5): Disintegration time of folic acid brands

Table no (5): Hardness test of folic acid tablet brand

Brand	**Hardness kg***
A	7.9
B	9.6

*Kg: kilogram

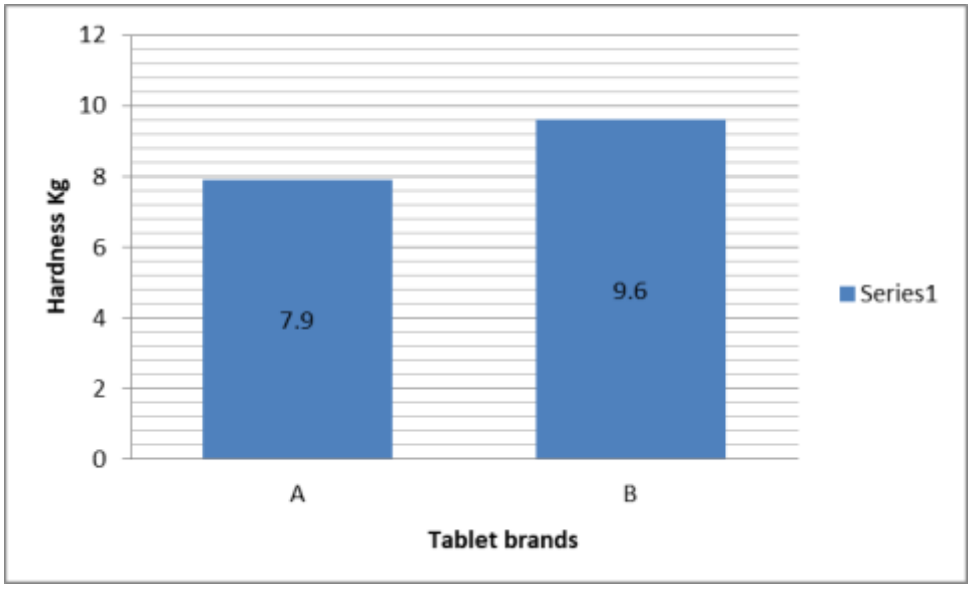

Figure no (6): Hardness test of folic acid tablet brands

Calibration curve of Standard Folic acid

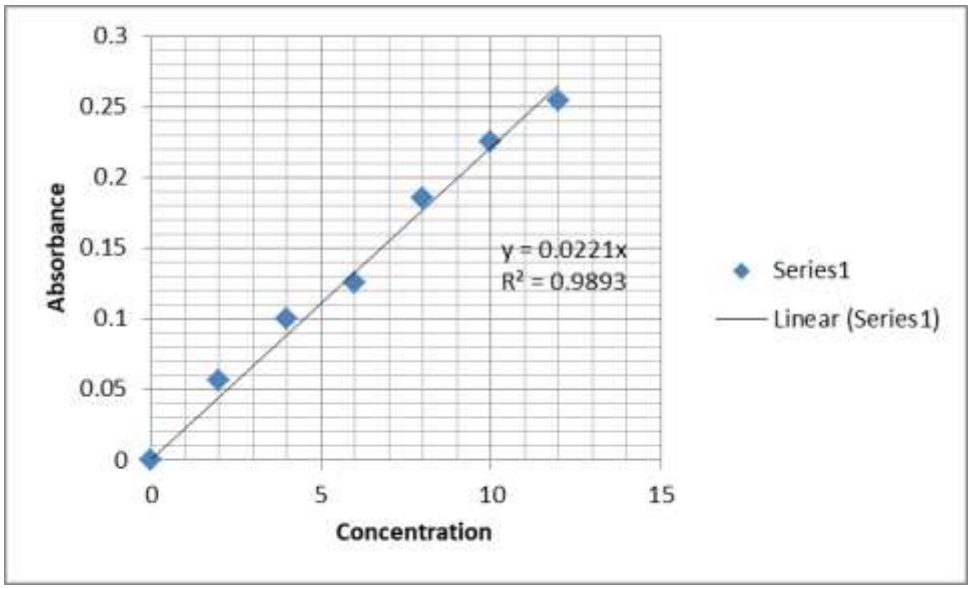

Figure no: (7) calibration curve of standard folic acid

Table no (6):In vitro drug release percentage of folic acid tablet brands

Time(minute)	Drug %release Brand A	Drug% release Brand B
10 min	76.4%	72%
15 min	85.6%	94.5%
30 min	94.9%	148.4%
45 min	105.8%	144%

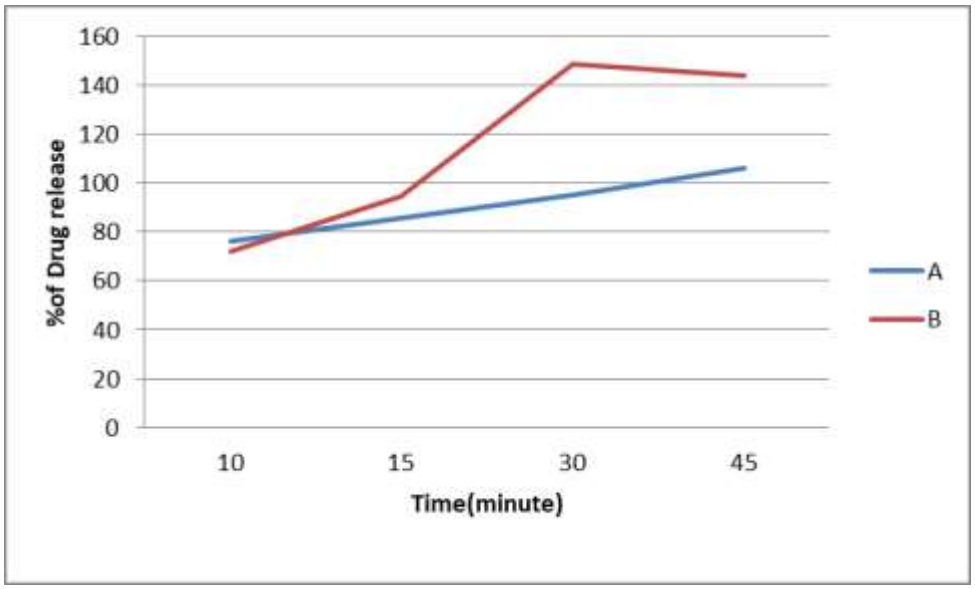

Figure no(8):In vitro drug release percentage of folic acid tablet brands

Table no (7):diameter and thickness of tablet brands.

Brands	Diameter	Thickness
A	7mm	4mm
B	7mm	4mm

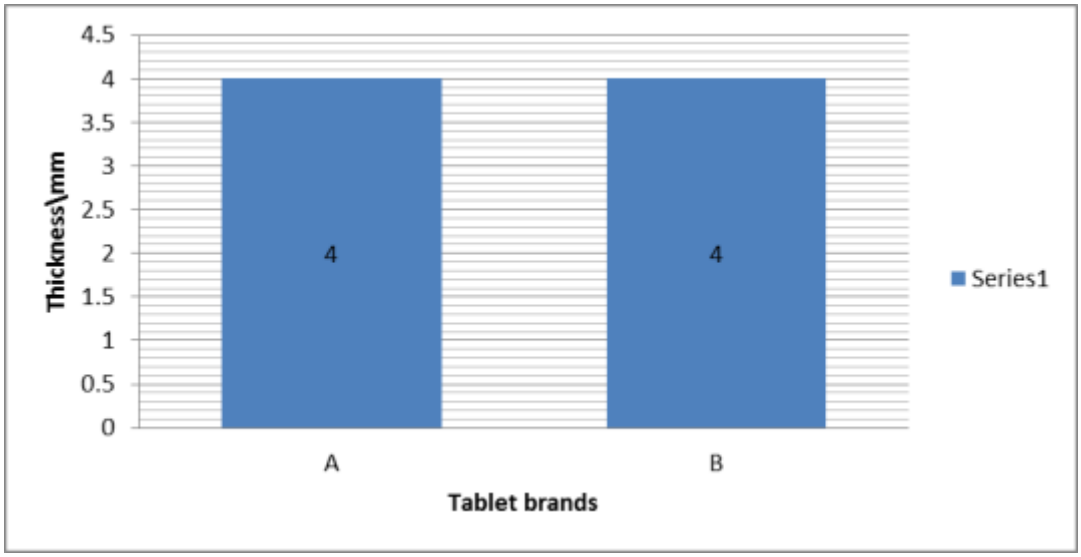

Figure no(9): Thickness of folic acid tablet brands.

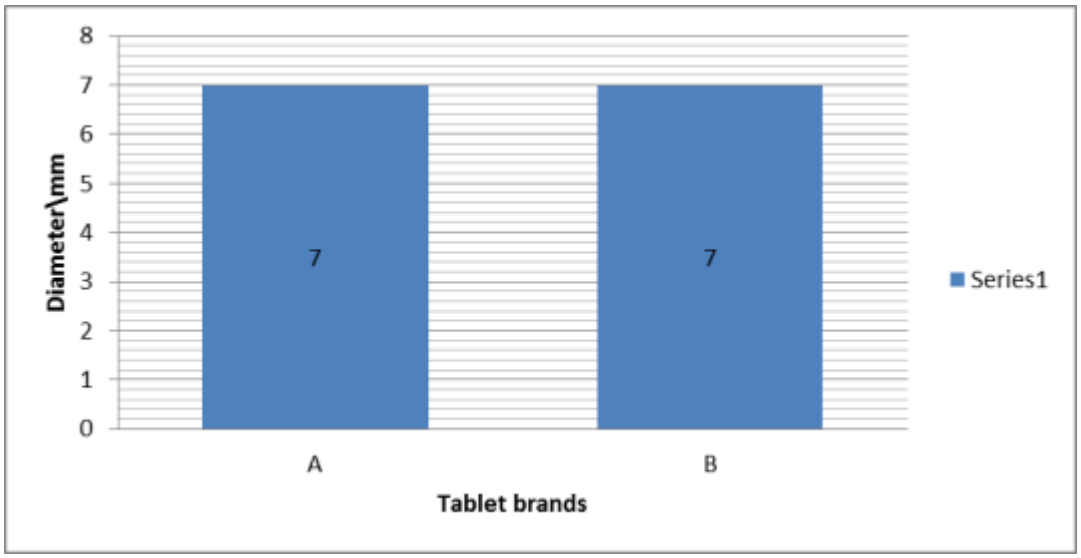

Figure no(10): Diameter of folic acid tablet brands

CHAPTER FOUR

Discussion ,conclusion ,Recommendation ,References

8. Discussion

weight variation test

Standard deviation test two tablet was evaluated for weight variation test brand A and brand B was 7.5 and 8 respectively comparing with the standard of pharmacopeia standard not exceed ± 10% it was acceptable. it is an important parameter because high weight variation indicates variation in amount of active ingredients and/or chemical additives. Variation of active ingredients may lead to toxicity, ineffectiveness or unpredictability of action of the product while variability of additives may affect other physicochemical characteristics of the product and ultimately alter the bioavailability of the drug.[31]

Friability test

Friability test two tablet was evaluated for test brand A and brand B was 0.86 and 0.86 both drug within the official limit of friability which is less than 1.0% according to British pharmacopeia was acceptable. Factors affecting the strength of tablets include the amount of binders used in granulation and the pressure applied during compression of the tablets. Friability test is closely related to tablet hardness and is designed to evaluate the ability of the tablet to withstand abrasion in coating, packaging, handling and transporting and other manufacturing processes. Generally, adequate tablet hardness as well as reasonable friability is required for consumer acceptance.[31]

Content uniformity

Content uniformity test two tablet was evaluated for test brand A and brand B was 102.4% and 100.8% they are all within limits which is from 95% to 105% according to BP. Assay for the content of active ingredients is a critical test of quality, as all the physical properties tested are meant to optimize release of the drug from the product. So, no matter how perfect a product may be in terms of physical parameters, failure to meet the standard for content of active ingredients will result in poor quality with adverse consequences.[31]

Disintegration Test

Disintegration Test two tablet was evaluated for test brand A and brand B Was 1.5 minute and 0.5 minute respectively and they are all within the official limits which is less than 15 minute according to British pharmacopeia. Factor affecting in disintegration test binders , lubricants ,hardness .were found to differ in their effects on disintegration.[32]

Hardness test

Hardness test two tablet was evaluated for test brand A and brand B was 7.9and 9.6 respectively comparing with the standard of British pharmacopeia 4 to 10 it was accepted. Factor that could affect the hardness of tablet the speed of compression, the flow and air entrapment also formulation variable process parameters.[33]

Dissolution Test

The calibration curve was built by charting concentration of folic acid versus absorbance .A linear relationship was Found between absorbance and the prepared concentration over the series of 4-50µg/ml. The dissolution test according to BP requires that not less than 75% of the active ingredient should dissolve within 45 minutes. All the tested products have satisfied this requirement and thus were in accord with the BP specifications However, it is uncertain if these differences in dissolution profiles of the different preparations might be reflected in their in vivo pharmacological effect. Brand B showed higher drug release percentage compared to brand A duo to factors affecting solubility include polymorphism, amorphous state and salvation, free base, or salt form, complications.[34]

tindinu endedn inenrneBini eiinBu ingnrdid in BedniB formulation and other solid dosage forms can distinctly eiiigB BSi diuudnrBidn of drug.[35]

9. Conclusion

All brands of immediate release folic acid tablets demonstrated elegant and attractive external features. Tablets were consistent in hardness, friability and weight. brands A and brand B exhibited sufficient mechanical strength to resist fracture and attrition. Additionally, these brands showed acceptable disintegration time and weight variation . Two brands of immediate release folic acid A" and "B" have been subjected to analysis according to the monograph of British Pharmacopoeia The results have shown that all the tested brands satisfied the BP requirements in terms of identification. Brand B which is the Sudanese one showed better distentegration and dissolution profile than brand A.

10. Recommendation

- Overall, it can be recommended that activation of the present regulations is required regarding the control of pharmaceutical products.
- Perhaps new regulations might also be necessary particularly concerning post marketing evaluation of the marketed products.

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