Formulation and evaluation of quality parameters of metronidazole 200mg and 400mg tablet

Submitted to:

DEPARTMENT OF PHARMACY
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LETTER OF APPROVAL

This Project, **"Formulation and evaluation of quality parameters of metronidazole tablet."** Submitted by **ID: 152-29-763** to the Department of Pharmacy, Daffodil International University, has been received as gratification for the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy and approved as to its mode and quantity.

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DECLARATION

I hereby declare that, this project report is done by me under the supervision of **Dr. Mohammed Shafikur Rahman**, Assistant Professor, Department of Pharmacy, Daffodil International University, within partial fulfillment from the requirements for that degree associated with Bachelor associated with Pharmacy. I'm declaring this Project is actually my unique work. I additionally declare which neither this particular project neither any component there for may be submitted elsewhere for that award associated with Bachelor or even any degree.

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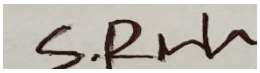

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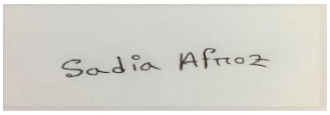

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Sadia Afroz
Author

Dedication

Dedicated To Almighty ALLAH

&

My parents

Also

My beloved Teachers

Who always support me and the one who brings out the best in me.

ABSTRACT

Metronidazole is a common antibiotic that is used to treat a wide variety of infections. It works by stopping the growth of certain bacteria and parasites. The aim of this study is to prepare a formula of metronidazole 200mg/ 400mg tablet and evaluate quality parameters of this products according to the United States Pharmacopoeia (USP) and the British Pharmacopoeia (BP) methods. Although the commercial price of this tablet is low, however, as the product is widely prescribed and consumed by huge number of poor patients, this study may find a more economical formulation that can obviously make an impression to patients. In this study the quality control parameters of formulated tablets were evaluated by doing weight variation test, hardness test, thickness, friability test, potency and dissolution by UV-spectroscopy following BP/USP criteria. The assay result and dissolution rate studies showed quite similar with other brand's tablet of metronidazole. By considering the result of the quality parameters the quality and efficacy of the newly formulated tablets were ensured and it may be marketed comparing metronidazole tablet.

Keywords: Metronidazole, weight variation, hardness, thickness, friability, assay, dissolution.

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Chapter One

Introduction

INTRODUCTION

1.1 Tablet

Tablets may be defined as the solid unit dosage form of medicament or medicaments with or without suitable excipients as well as prepared possibly by molding or even by compression. Strong medicaments perhaps administered by mouth as powders, tablets, cachets, capsule or pills. These dose forms have a quantity associated with drug that is given like a single unit plus they are known with each other as solid unit dose forms, even regarding sustained motion preparation that technically include equivalent associated with several regular dosage associated with drug.

Tablet tend to be solid dosage type containing a number of active component prepared possibly by compression or molding method as well as suitable excipient.
Based on Indian pharmacopoeia, Pharmaceutical drug tablets tend to be solid, concave or even biconvex meals solid dosage type, prepared through compressing the drug or a combination of drugs along with or without having diluents.

1.2 Important criteria of the good tablet:

1. Precise and standard weight
2. Uniformity from the shape and size
3. The drug ought to be uniformly distributed within the tablet
4. Absence associated with incompatibilities
5. Should not too hard to disintegrate
6. Satisfying appearance
7. Should be economic
8. Balance and solidity

1.3 Advantages of tablet

1. Big scale manufacturing
2. Economical
3. Self-administration can be done
4. Wide range
5. Simple packaging
6. Simple to transport
7. Product identification is simple
8. It may be store inside a normal heat
9. Lighter in weight and small
10. Greater microbial as well as chemical stability total dosage type

1.4 Disadvantage of tablet

1. Inappropriate in emergency situation
2. Difficult to shallow in case of children and unconscious patient
3. Higher dose as well as poorly compressible
4. Slow beginning of motion
5. Poor wetting API can't be compressed
6. Very first pass metabolic process occur
7. Bitter screening and uncomfortable odor can't be mask

1.5 Different types of formulation:

- Tablets: Immediate-release, Sustained-release, Delayed-release, Film-coated.
- Capsules: Powder, Granule filling.
- Pellets: Into tablets or Capsule filled.
- Powders: Powder in a bottle.
- Oral and Parenteral Liquids: Solutions, Suspensions, Emulsions.
- Semi-solids: Creams, Ointments, Gel, lotion.

1.6 Factors that affect to select a dose form for any particular medication substance:

1. Grow older of individual (Pediatric/Geriatric)
2. Condition of illness (acute or even chronic)
3. Group of disease (Infections, most cancers, psychiatrics...)
4. Pharmacokinetic guidelines (half-life, very first pass metabolic process, bioavailability)
5. Salt type of drug material
6. Cost as well as duration associated with therapy

1.7 Factors that needed for the formulation of tablet:

1. 5-10% API
2. 80% of Excipient
3. 10% of the compound which ensure easy disintegration, disaggregation and dissolution of tablet.

Chapter two

Literature Overview

METRONIDAZOLE

Metronidazole (MTR), is 2-(2-methyl- 5-nitro-1H-imidazol-1- yl) ethanol [Figure-1]. Metronidazole is really a commonly utilized antibiotic broker. Metronidazole is definitely an antibiotic which successful towards anaerobic germs and particular parasites. Anaerobic bacteria could cause disease within the liver (liver abscess), abdomen (bacterial peritonitis) and pelvis (abscess from the ovaries and also the Fallopian tubes). Giardia lamblia as well as ameba tend to be intestinal parasites that may cause stomach pain as well as diarrhea within infected people [1]. Metronidazole selectively blocks a few of the functions inside the bacterial cells and also the parasites leading to their passing away.

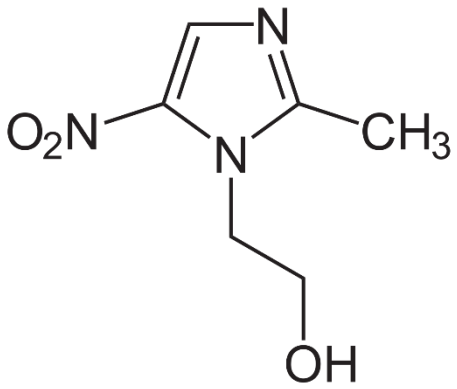

Figure-1: Metronidazole.

Molecular Formula: $C_6H_9N_3O_3$

Chemical names: (l-β-hydroxyethyl)-2-methyl-5-nitroimidazole

Molecular weight: 171.156 g/mol.

Trade name: Flagyl, Metro.

It can be used for numerous conditions for example protozoal actions (for instance, giardiasis) anaerobic transmissions, Helicobacter connected gastritis, as well as hepato-encephalopathy. Based on Previous reviews metronidazole toxicity might induce a number of neuroloic unwanted effects, including ataxic stride, peripheral neuropathy, dysarthria, encephalopathy as well as seizures [2].

2.1 Uses of metronidazole tablet

Metronidazole is definitely an antibiotic that's used to deal with a multitude of infections. It functions stopping the actual growth associated with certain germs and unwanted organisms.

This antibiotic goodies only particular bacterial as well as parasitic bacterial infections. It won't work with regard to viral bacterial infections (such because common chilly, flu). Using any kind of antibiotic when it's not required can make it not work with future bacterial infections.

Metronidazole could also be used with additional medications to deal with certain stomach/intestinal ulcers the result of a bacteria (H. pylori).

2.2 Side effects of metronidazole tablet

Dizziness, stomach upset, headache, nausea, vomiting, loss of appetite, diarrhea, constipation, or metallic taste inside your mouth might occur. If these effects final or worsen, tell your physician or druggist promptly.

This medication could cause your urine to show darker within color. This impact is harmless and can disappear once the medication is actually stopped.

Remember that the doctor offers prescribed this particular medication because she or he has judged how the benefit for you is more than the danger of unwanted effects. Many people by using this medication don't have serious unwanted effects.

2.3 Precautions

Before getting metronidazole, tell your physician or pharmacist if you're allergic into it; or in order to other antibiotics (such because tinidazole); or for those who have any additional allergies. The product may include inactive elements, which may cause allergic responses or additional problems. Speak to your pharmacist for additional information.

Before by using this medication, tell your physician or druggist your health background, especially associated with: liver illness, kidney illness, certain bloodstream disorders (low bloodstream cell counts).

Avoid alcohol based drinks and items containing propylene glycol whilst taking this particular medication as well as for a minimum of 3 times after completing this medication because serious stomach upset/cramps, nausea, vomiting, headache, and flushing may occur.

2.4 Interactions

Medication interactions might change exactly how your medicines work or even increase your own risk with regard to serious unwanted effects. This document doesn't contain just about all possible medication interactions. Keep a summary of all these products you make use of (including prescription/nonprescription medicines and natural products) as well as share it together with your doctor as well as pharmacist. Don't start, cease, or alter the dose of any kind of medicines without having your physician's approval.

Some products that could interact with this particular drug consist of: alcohol-containing items (such because cough as well as cold syrups, aftershave), items containing propylene glycol, lopinavir/ritonavir answer, lithium.

Chapter Three

Methods and Materials

3.1 Formulation

3.2 Formulation of core tablets of metronidazole 200mg:

In this study metronidazole 200/400 mg tablet was formulated according to USP limits of active pharmaceutical ingredient and excipients use. Here most economical and quality full API and excipients were used [Table-1 and Table-2].

Table-1: Metronidazole 200mg formula.

Ingredients	**Function**	**Quantity (mg)**	**Tk**	**%**
Metronidazole	API	200 [2]	**0.228**	36.366
Lactose	Diluent	278.5 [3]	**0.125**	50.64
starch paste(maize-starch)	Binder	44 [4]	**0.00123**	8
Magnesium stearate	lubricant	17.5 [5]	**0.00157**	3.18
Talc	Glidant/ lubricant	10 [6]	**0.00018**	1.814
	total	550	**0.355**	100

3.3Formulation of core tablets of metronidazole 400mg:

Table-2: Metronidazole 400mg formula.

Ingredients	**Function**	**Quantity (mg)**	**Tk**	**%**
Metronidazole	API	400	**0.456**	60.606
Lactose	Diluent	174.205	**0.0781**	26.394
starch paste(maize-starch)	Binder	52.8	**0.00147**	8
Magnesium stearate	lubricant	20	**0.0018**	3.0303
Talc	Glidant/ lubricant	13	**0.000234**	1.969
	total	660	**0.537**	100

The manufacturing price of metronidazole 200 mg is around 0.355 tk or 0.00443 USD per tablet and metronidazole 400 mg is around 0.537 tk or 0.00671 USD per tablet.

3.4 Preparation procedure of metronidazole

The core tablets (average weight 550 mg/660 mg) of metronidazole were prepared by wet granulation technique. Wet granulation (involving moist massing) wet granulation entails the massing of a mixture of dry main powder particles utilizing a granulating fluid (the procedure for adding the liquid means to fix powders). The fluid includes a solvent which should be volatile in order that it can end up being removed through drying, and become non-toxic [8].

Procedure:

1. Dispensed API and excipients accurately.
2. Sieved API and excipients by sieve pan.
3. Then mixed Metronidazole, Lactose by mortar and pastel.
4. On the other hand, prepared starch paste – maize starch boiled with purified water. Then paste cooled below the 40ºc.
5. Next starch paste mixed with Metronidazole, Lactose mixer for making granules.
6. Then granules dried using dryer 100ºc for 30 minutes.
7. Then sieved the dried granules
8. Then lubricant and glidant were used with granules and blended the mixer.
9. Then compressed and prepared tablet.
10. This process applied upon both two hundred mg as well as 400 mg pill individually.

Figure 2: Mixing ingredients.

Figure 3: Granules of metronidazole.

Figure4: Compression process of metronidazole.

Figure 5: Tablets of metronidazole.

3.5 Tablet specifications

All parameters (weight variation, thickness, hardness and friability) of prepared tablet of metronidazole 200mg/ 400mg were completed and outcomes showed that they're in compliance with BP/USP limitations.

3.6 In vitro quality control tests:

3.7 Weight variation test

Average weight of tablet (mg)	% Difference allowed
130 or less	10 %
From 130 to 324	7.5 %
> 324	5 %

The actual weight variance test is really a satisfactory approach to determining the actual medicine content material uniformity associated with tablets as well as does serve like a pointer in order to good production practices (GMP) maintained through the manufacturers along with the amount associated with active pharmaceutical drug ingredient (API) included in the formulation. Ten tablets from every brand items were considered individually inside a weighing stability. The typical weights from the tablet, in addition to their % deviation, had been calculated (Table 3) utilizing following formula [9].

Figure 6: Balance machine.

Weight variation = (Iw − Aw)/Aw × 100%

Where, Iw = Individual weight of the tablet and Aw = Average weight of the tablet.

3.8 Thickness test

Thickness of metronidazole including average, relative standard deviation, upper as well as lower limitations are prior to BP/USP.

Figure 7: Vernier caliper.

3.9 Hardness test

Hardness test of metronidazole tablets was found to become with the stated recommendations as provided in BP/USP. Similarly the state range associated with hardness mentioned in BP/USP is no less than 4. 00 Kg associated with pressure is needed to break the tablet as well as we found all of the samples were prior to the Restrict [2].

Figure 8: Monsanto Type Tablet Hardness Tester.

3.10 Friability test

This test is supposed to look for the friability associated with uncoated tablets, the phenomenon whereby tablet areas are broken and/or show proof of lamination or even breakage when put through mechanical surprise or attrition. (BP 2000). Friability associated with tablets was no less than 1%. It is therefore not compliance using the BP/USP regular.

Figure 9: Friability Tester.

3.11 Preparation of standard curve

A series of standard solution of Metronidazole standard eg, 50µg/mL, 25µg/mL, 12.5µg/mL, 6.25µg/mL, 3.125µg/mL, 1.56µg/mL etc were prepared and absorbance was measured at 277nm against a blank for each solution by uv-spectrophotometer. The actual calculated absorbance had been plotted from the particular focus from the regular methods to examine the actual linearity.

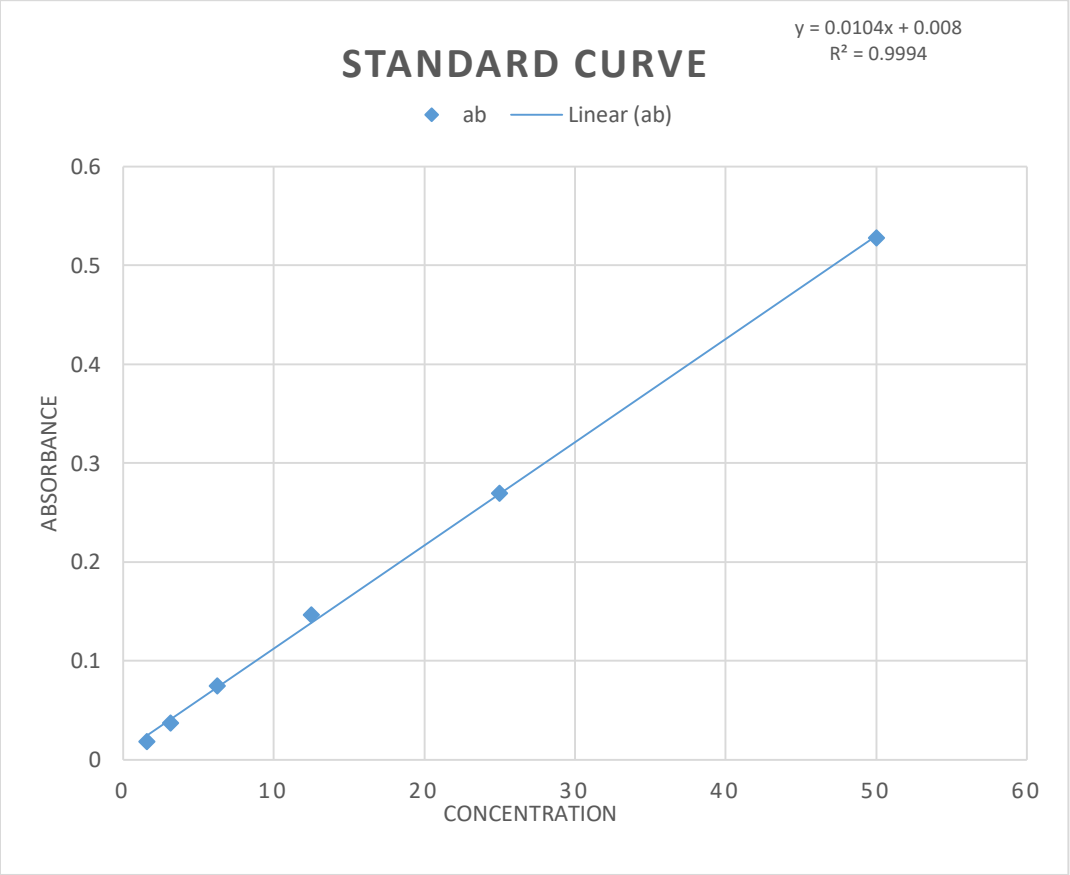

Figure 10: Standard curve of metronidazole tablet.

3.12 Dissolution test

Dissolution test of tablets was performed by using basket method. About 900 ml of .1N HCL was filled into 1000 mL basket of dissolution apparatus. One metronidazole tablets was placed into each basket. The dissolution medium was heated up to (37±0.5) ˚C by an auto heater and 100 R.P.M was adjusted. 5ml solution was withdrawn from beaker at 10 minutes interval which was replaced with 5ml distilled water & then withdrawn solution was filtered through filter paper. The

withdrawn solution of the sample was suitably diluted & absorbance was measured at 277nm by using UV-visible spectrophotometer against blank [10]

Figure 11: Dissolution test.

3.13 Assay test

This particular test is conducted to look for the amount associated with API inside a dosage types. This check determines the actual strength or even content from the API within the pharmaceutical tablet and it is sometimes known as a content material test. An assay is definitely an investigative (analytic) process in lab medicine, pharmacology, environmental the field of biology and molecular the field of biology for qualitatively evaluating or quantitatively calculating the existence or quantity or the actual functional activity of the target organization [2].

Chapter Four

Result and Discussion

4.1 Weight Variation

Table 3.1: Weight Variation of metronidazole 200 mg tablet

Sl.no.	**Wt. of tablet (mg)**	**Average wt. (mg)**	**Wt. Variation** (%)	**RSD %**
1	550	558	1.433	1.755
2	550		1.433	
3	580		3.942	
4	560		0.358	
5	570		2.150	
6	560		0.358	
7	550		1.433	
8	550		1.433	
9	560		0.358	
10	550		1.433	

Comments: All individual wt. meet the range.

Table 3.2: Weight Variation of metronidazole 400 mg tablet

Sl.no.	**Wt. of tablet (mg)**	**Average wt. (mg)**	**Wt. Variation** (%)	**RSD %**
1	670	653	2.603	2.171
2	680		4.134	
3	640		1.990	
4	670		2.603	
5	650		0.459	
6	640		1.990	
7	650		0.459	
8	650		0.459	
9	640		1.99	
10	640		1.990	

Comments: All individual wt. meet the range.

4.2 Assay

The assay in the release is ± 5% according to the USP [11]

Sample	**Assay %**
metronidazole 200mg	96.45
metronidazole 400mg	97.02

4.3 Hardness Test

Table 4.1: Hardness of metronidazole 200mg tablet

Sl.no.	**Hardness(Kg/cm)**	**Average Hardness(Kg/cm)**
1	3.1	3.12
2	3.2	
3	3.1	
4	3	
5	3.1	
6	3.2	
7	3.1	
8	3.1	
9	3.2	
10	3.1	

Comments: All individual hardness meet the range [it's acceptable depend on drug relase]

Table 4.2: Hardness of metronidazole 400mg tablet

Sl.no.	**Hardness(Kg/cm)**	**Average Hardness(Kg/cm)**
1	4.7	4.65
2	4.5	
3	4.7	
4	4.6	
5	4.7	
6	4.6	
7	4.6	
8	4.7	
9	4.7	
10	4.7	

Comments: All individual Hardness meet the range [it's acceptable depend on drug relase]

4.4 Thickness Test

Table 5.1: Thickness test of metronidazole 200mg tablet

Sl.no.	Thickness (cm)	Average thickness (cm)
1	1.25	1.25
2	1.25	
3	1.25	
4	1.25	
5	1.25	
6	1.25	
7	1.25	
8	1.25	
9	1.25	
10	1.25	

Comments: All individual Thickness meet the range.

Table 5.2: Thickness test of metronidazole 400mg tablet

Sl.no.	Thickness (cm)	Average thickness (cm)
1	1.27	1.27
2	1.27	
3	1.27	
4	1.27	
5	1.27	
6	1.27	
7	1.27	
8	1.27	
9	1.27	
10	1.27	

Comments: All individual Thickness meet the range.

4.5 Friability Test result

This test is additional to check crushing strength of tablet by this test one can check Capping &/or Lamination. **USP limit** is 0.5 to 1%. Rotation: - 25 rpm or 100 rotations in 4 min [12]

Name	Result of friability
metronidazole 200mg	0.305%

metronidazole 400mg	0.413%

Comments: Friability meet the range.

4.6 Dissolution test

Table6.1 Dissolution rate for 200mg metronidazole.

Sample	time	Absorbance	% drug release
200mg metronidazole.	After 15 minutes	0.412	53.4
	After 30 minutes	0.506	65.6
	After 45 minutes	0.613	79.5
	After 60 minutes	0.708	91.8

Table6.2 Dissolution rate for 400mg metronidazole.

Sample	time	Absorbance	% drug release
400mg metronidazole.	After 15 minutes	0.249	47.8
	After 30 minutes	0.318	61.1
	After 45 minutes	0.427	82.0
	After 60 minutes	0.509	97.7

Chapter Five

Conclusion

CONCLUSION

With this study, an effort has been designed to formulate metronidazole with low cost and all result of this study shown positive result. In this study also ensured the quality of this economical tablet. Metronidazole is really a poorly water soluble medication. Due in order to its bad solubility it's very difficult in order to achieve preferred bioavailability. The life span of someone relies upon the medication he/she is actually taking must be safe and also have good effectiveness. So all of us did numerous official as well as non-official as well as in-vitro research like weight variation, friability, solidity, dissolution as well as potency assessments. Based on this evaluation, new developed tablet associated with metronidazole contain top quality and great efficacy through passing all of the pharmacopoeia needs. Bioavailability as well as therapeutic effect depends upon these high quality control assessments. So, it's important to assess different tablet parameters correctly before advertising. These kinds of studies ought to be conducted more often not and then build open public awareness about the caliber of marketed pharmaceutical drug products but additionally because these kind of studies are extremely helpful for that betterment associated with pharmaceutical field.

Chapter Six

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THANK YOU