FORMULATION AND EVALUATION OF PUMPKIN SEED(*Cucurbita pepo*) TABLETS

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REG. NUMBER: U53/69847/ 2013

A dissertation submitted in partial fulfillment of the requirements for the award of Master of Pharmacy degree in Industrial Pharmacy of the University of Nairobi.

DECLARATION

I Josephine K. Mbondo hereby declare that this is my original work and it has not been presented for the award of any degree in any other institution.

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DEDICATION

This work is dedicated to my Children Michelle Mumo, Allan Muuo, and Aaron Nzomo, You have taught me patience, how to love unreservedly and without counting the cost. To you I will always remain mom. A tittle that gives me much honour and great joy.

ABBREVIATIONS AND ACRONYMS

ADI	Acceptable daily intake
BP	British Pharmacopoeia
CI	Compressibility index
CCS	Crosscarmellose sodium
cm	Centimetre
C. Pepo	*Cucurbita Pepo*
^{o}C	Degrees Celsius
Db	Bulk density
Dt	Tapped density
DT	Disintegration Time
FDA	Food and Drug Administration
g	grams
HR	Hausner ratio
PVP	polyvinyl pyrolidone
QC	Quality control
rpm	Rotations per minute
ɵ	Angle of repose
Vo	Bulk volume
µm	Micrometres
WHO	World health organization

DEFINITION OF TERMS

Excipient: Inactive substances incorporated into a drug product.

Super disintegrant: an excipient added to a tablet to aid in fast disintegration

Disintegration test: Determines time taken for tablets and capsules to disintegrate when placed within a specified liquid medium under given experimental conditions

Compressibility: Ability of powder to decrease in volume under pressure

Bulk density: Ratio of mass of untapped powder sample and its volume including void volume

Tapped density: The ratio of a mass of tapped powder sample and its volume obtained after mechanically tapping the container containing the powder sample.

Hausner ratio: It is a measure of the interparticulate friction of powder particles /granules

Acceptable daily intake: Amount of certain ingredient that is recommended to be taken per day

Formulation: The systematic combination of drug product and excipients to produce a dosage form that meets specified quality criteria.

Tablet hardness test: Measures the mechanical strength of a tablet and its structural integrity.

Friability test: Measures the percentage weight loss by tablets due to chipping and abrasion caused by mechanical stress.

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ABSTRACT

The use of herbal medicines in management of medical conditions has become popular in the recent years both for preventive and curative purposes. With the increasing prevalence of certain diseases eg. Benign Prostate Hyperplasia, diabetes, arthritis and the accompanying economic burden, it is prudent to venture in the development of new safer and inexpensive medicines for their management. Pumpkin seeds have been used for the management of these and other medical conditions. The seeds of pumpkin are normally powdered for administration or chewed whole. This mode of administration poses limitations such as inaccurate dosing due to variation of measuring devices used. Due to the bulkiness of powders and seeds further makes them inappropriate to carry especially during travel. The presence of oils in the powders also increases the possibility of rancidity due to variations in storage conditions of the powders. There is also a high potential of microbial growth especially when powders are mixed with other food ingredients for the purpose of making porridge. Since this powders are subjected to high temperatures during the process of cooking, there is therefore a high likelihood of the active ingredients getting inactivated by high temperatures used. Powders are also prone to adulteration hence formulation into a tablet decreases this possibility. In the present research work, tablets of pumpkin seed were prepared by the wet granulation technique. The purpose of this was to formulate a suitable solid dosage form of whole pumpkin seed that may address the above mentioned limitations. Pre-formulation studies indicated that the powder did not have free flowing capacity and hence wet granulation method was adopted. The tablets were evaluated for hardness, weight variation, friability, and disintegration time. From the results, it was concluded that tablets can be made from pumpkin seed powder which will improve effectiveness and patient compliance.

Pumpkin seeds were obtained from Nakumatt Mega supermarket in Kenya, other excipients were obtained from Department of Pharmaceutics and Pharmacy Practice Laboratory. Three formulations (F1-F3) in which the choice of binder and disintegrant were varied were prepared
F1 contained corn starch 10% binder and crosscarmellose 5% disintegrant. F2 contained sucrose 10% binder and polyvinylpyrollidone 5% disintegrant. F3 contained polyvinyl pyrollidone 10% binder and cornstarch 5% disintegrant. (% w/w of total tablet weight)

The equipment used included Single punch tablet compression machine (Erweka, electric type, Germany) Disintegration Tester Machine (Erweka ZT3, GmbH Heusenstamm, Germany) Friability Tester machine (Erweka, Heusenstamm, type TA3R, German) and tablet Hardness Tester (Scheuniger, electric type, Germany), Weighing balance (Shimadzu), Vernier calipers.

From the preformulation studies, *C.pepo* powder had a D_b of 0.35 and D_t of 0.56. The Hausner ratio obtained was 1.6. The compressibility index was very poor 38%. The angle of repose was 34. Tablets of all formulations passed the uniformity of weight test. Two formulations passed the Friability and hardness test (F1 and F2) while formulation F3 failed both tests. Only one formulation F1 displayed good disintegration time profile of 14 minutes. Both F2 and F3 displayed prolonged disintegration time more than 15 minutes recommended for uncoated tablets. In conclusion this study indicated that uncoated tablets of pumpkin seeds can be formulated using cornstarch singly as a binder and crosscarmellose as disintegrant. In the case of sucrose binder further research is recommended to optimize the disintegration time. The general appearance of tablets was good for all formulations. Further research is also recommended to establish clinical data for treatment with *C. pepo* tablets before scale up for commercial production can occur.

CHAPTER ONE: INTRODUCTION

1.1 BACKGROUND STUDY

Pumpkin(*Cucurbita pepo)* is a plant that has been traditionally used as a medicine in developing countries and obtained resurgence of use in the united states and Europe(Caili et al., 2006). Edible parts of the plant include the flowers, fruit, leaves, root and the seeds. Pumpkin is cultivated throughout the world and traditionally used as medicine in China, Yugoslavia, Argentina, India, Mexico, Brazil and America. In various systems it has been utilized for various ailments eg Antidiabetic, antihypertensive, antitumor,immunomodulation,antibacterial, antihypercholesterolemia, intestinal antiparasitia, antiinflamation, antalgic (Caili et al., 2006).

For traditional medicine purposes the seeds are normally the ones used and are presented as dry powders or the dried seeds are normally chewed for treatment of various ailments. There is no available literature on formulation studies to facilitate the production of quality solid dosage forms. The purpose of this study was to formulate a suitable pumpkin seed (*C. pepo)* tablet.

Extracts of pumpkin (*Cucurbita pepo*) seeds have been used in Europe as folk medicine for remedy for micturition problems caused by prostate. The exact mechanism of Curbicin is not clear but it has been shown to decrease the binding capacity of androgen receptors to testosterone(CARBIN et al., 1990). Curbicin appears to have a dual action in influencing the development of prostatic hyperplasia. The competitive binding of phytosterols to androgen receptors owing to their similarity in structure to androgens and oestrogens(CARBIN et al., 1990).

According to the WHO monograph volume 4 the dried seed are described as ovate, constricted at one end forming a short, blunt extension; flat or weakly biconvex; upto 25mm long and 8-14mm wide, 3-4mm thick on both faces, close to the edge,is an encircling ridge and groove, 1-2 mm wide. The organoleptic properties are described as having an indistinct odour, bland taste oily and slightly nut like taste.

According to the monograph, the major constituents include a fixed oil (30-53%),
phytosterols (1%) and terpenes.

1.2 PROBLEM STATEMENT

The use of herbal medicines in management of medical conditions has become popular in the recent years. Pumpkin seeds have been used either as seeds for chewing or as powders for the management of many medical conditions. These powders are prone to adulteration and rancidity. The use of powders and seeds also poses inconvenience due to bulkiness and inaccuracy of measurement resulting in inaccurate dosing. To counter this problem, the powdered seeds can be compressed into tablets.

As precision of dosing and patients compliance are necessary in long term management of disease, then there arises a need to develop a formulation which is easily accessible and convenient to enhance patients acceptability and adherence to treatment.

Mostly pumpkin seed powders are usually dispersed into liquids e.g. Porridge, milk, honey prior to oral administration. In this case there is no clear dose regulation. This problem is compounded by the absence of uniform measuring devices used in most households.

In other instances the seeds are prescribed for chewing as snacks in which case a handful of seeds are prescribed every week. This kind of prescription still results in variations of measurement well as unpredictable variations in treatment outcomes.

The storage of powders is also inconvenient due to bulkiness and the variations of storage conditions can result in rancidity of the oils present. Formulating the powder into tablets increases stability.

This study therefore, aimed at developing tablets of *C. pepo* whole seed powder in an attempt to address the above stated problem.

1.3 OBJECTIVES

1.3.1 GENERAL OBJECTIVE

To formulate and evaluate pumpkin seed *(Cucurbita pepo*) powder into tablets in order to improve consumer acceptability, ease of dosing and compliance.

1.3.2 SPECIFIC OBJECTIVES

- To carry out pre-formulation studies on the seed powder
- To granulate Pumpkin seed (*Cucurbita pepo)* powder
- To compress granules into tablets
- To evaluate the quality of the formulated tablets

1.4 SIGNIFICANCE AND ANTICIPATED OUTCOME

The tablets are expected to be formulated and presented in a manner that allows consumers to access them in a form more suitable for use as well as in a form that is free from microbial contamination. This will help address the problem of bulkiness of powder storage and inconvenience of chewing seeds. The tablets will also improve ease of dosing for consumers as well as improve and increase acceptability. The use of tablets will also facilitate and improve monitoring of treatment outcomes.

1.5 DELIMITATION

Preformulation was limited to physical characterization of pumpkin seed powder. This included determination of Hausnerôs ratio, bulk density, tapped density, angle of repose and compressibility index.

1.6 LIMITATIONS

Long term stability of the formulated tablets was not done since this requires that they are stored for a length of time and their quality monitored at specified periods, this amount of time was not possible in the study period that was available.

There are limited studies done to determine the dosage of pumpkin seed powder for administration. Available studies indicate dosage for the oily extract only and this was considered in determining the current dosage strength prepared.

CHAPTER 2: LITERATURE REVIEW

Plate 1: Pumpkin fruit and seeds

The pumpkin has both nutritional and health protective value of considerable importance. It belongs to the family of angiosperms and genus *Cucurbita* with different varieties. One fruit has about 500 seeds which are interspersed in a net like structure called mucilaginous fibers present at its inner cavity(ADEEL et al., 2014).

Traditionally in Mexico and the U.S pumpkin seeds and its oil have been used as antihelmintic that kills and aids in the expulsion of parasitic worms(Aruah et al., 2012) treatment of bladder disorders, vermifuge and diuretic seeds. Supplementation of pumpkin seeds snack gave a higher level of inhibitor of crystal formation or aggregation which subsequently reduces the risk of bladder stone disease (Suphiphat et al., 1993).pumpkin seeds 60mg/kg(body weight per day could reduce the incidence of bladder stone. The longer the duration of supplementation the better the results. Pumpkin is widely studied with regard to its anti-diabetic effect and the fruit pulp and seeds of the plant have shown hypoglycemic activity in normal animals and alloxan induced diabetic rabbits (Caili et al., 2006). Reduction in blood glucose, serum total cholesterol and triglyceride was observed in alloxan induced diabetic rabbits applied with pumpkin powder.

Hypoglycemic activity of water extracted pumpkin polysaccharides was demonstrated and excelled glibenclamide in alloxan induced diabetic rats. Some studies have also shown that the oil prevents diabetic nephropathy due to presence of phytochemical compounds. The role of pumpkin in diabetes is paramount importance as it serves various purposes in the patient eg. Reducing blood sugar, increasing the insulin level, and decreasing the branched chain amino acids. Pumpkin also having di-hydro-epiandrosterone blocking actions which helps in ovarian and prostate cancer(CARBIN et al., 1990). Blood pressure lowering effect, cardiac protection, antioxidant effect, antifungal, antidiabetic, antibacterial, antihypercholesterolemic, and anti-inflammatory. The seeds and oil have also been claimed to help in curing HIV/AIDS(Zimmerman, 1997). The antimicrobial activity has many applications including preservation, pharmaceuticals, alternative medicine and natural therapies(Rajakaruna et al., 2002). Broadspectrum Antibacterial activity has been observed with extracts. The oil inhibits acinebacter baumanii, Aeromonas veronii, Candida albicans, enterococcus faecalis, Escеherichia coli, klebsiella pneumonia, pseudomonas aeruginosa, Salmonella enterica sub species,Serratia marcescens, and staphylococcus aureus at concentration of 2% (v/v). A peptide from of molecular weight 8kDa from pumpkin seeds was proved to inhibit B. cinerea, Fusarium oxysporum,M. arachidicola at a dose of 375µg and exerted an inhibitory effect on cell free translation with IC50 of 1.2µM.

ANALYSIS OF PUMPKIN SEED AND ITS OIL (Adeel et al, 2014)

The Shelf life of pumpkin seeds is inversely proportional to the moisture content. The crude protein and oil in its seeds are 20% and 22% respectively(ADEEL et al., 2014). Further analysis of the seed oil shows that it contains different fatty acids and linoleic acid is present in the highest amount i.e 48%, oleic acid 34%,high amount of unsaturated fatty acids which make it a good source for human consumption(ADEEL et al., 2014). The oil also shows good antimicrobial activity against *S. aureus*. A study comparing its activity against a control of ampicillin showed approximately same inhibitory action which indicates its suitability in food and pharmaceutical drugs(ADEEL et al., 2014).

The fatty acid profile as identified by Gas chromatography(ADEEL et al., 2014) is as shown in table below.

Table 1: Composition of Pumpkin seed oil

Name of compound	**Structural formula**	**% w/w**
Palmitic acid methyl ester	$CH_3(CH_2)_{14}COOH$	16.36
Stearic acid methyl ester	$CH_3(CH_2)_{16}COOH$	9.2
Oleic acid methyl ester	$CH_3(CH_2)_7CH=CH(CH_2)_7COOH$	34.27
Linoleic acid methyl ester	$CH_3(CH_2)_3(CH_2CH=)_2(CH_2)_7COOH$	48.02
Linolenic acidmethyl ester	$CH_3(CH_2CH=CH)_3(CH_2)_7COOH$	0.17

In this study raw powder of pumpkin seeds was used to prevent variability. Pre-formulation studies were done to evaluate pre-compression parameters of the raw powder to determine feasibility of direct compression. Granulation was carried out to improve powder characteristics. Tablets were prepared using a hand operated single punch tablet press and evaluated for post compression parameters i.e. general appearance, uniformity of weight, hardness, friability, and disintegration.

According to community herbal monograph on Cucurbita pepo, it is listed as having been used traditionally for the relief of lower urinary tract symptoms related to benign prostate hyperplasia or overactive bladder.

The recommended doses of the herbal comminuted substance for adults and the elderly is 2.5 ï 7.5g taken twice daily.

For the soft extract the recommended dose is 500mg taken twice daily. For the dry extract single dose 105 mg taken three times daily. For the fatty oil a single dose is recommended of 1-1.2g taken 3 times daily or a daily dose of 3-4g.

According to a study by (Sicilia et al., 2002) the active principles in the pumpkin seeds include, Triterpenoids (Cucurbitacins), carotenoids, Fatty acids, Minerals, Tocopherols and Lignans.

Applications in herbal therapy as listed in the monograph include: As an antihelmintic especially against worms of the genera Ascaris, Taenia and oxiuris (Younis et al., 2002), the seeds are also used against benign prostate hyperplasia (BPH) sometimes in conjunction with other herbs, especially saw palmetto (*Serenoa repens*) seed extract (Dreikorn, 2002), to treat prostate cancer (Yarnel et al., 2003) to treat irritable bladder (Leung and Foster, 1996).

Several clinical studies have been carried out employing pumpkin seeds. Examples include a multicenter controlled study involving more than two thousand subjects in which a product containing pumpkin seeds was evaluated for treatment of BPH. The results indicated that the seeds were effective in reducing symptoms associated with BPH especially in its early stages and also there were no side effects of note reported by the patients (Friederich et al., 2000).

Pumpkin seed oil has also been shown to poses strong antioxidant properties in animal experiments (Fahim et al., 1995). Clinical research in thailand has shown that pumpkin seeds increase the level of inhibitors of crystal formation or aggregation that reduce the risk of bladder stone disease (urolithiasis) (suphiphat et al., 1993; Supharkan et al., 1987)

In all the studies conducted there were no reports of serious adverse effects.

CHAPTER 3: MATERIALS AND METHODS

3.1 STUDY DESIGN

This was an experimental Laboratory based study.

3.2 STUDY LOCATION

The study was carried out in the laboratory at the School of Pharmacy, in the department of Pharmaceutics and Pharmacy Practice, University of Nairobi, Kenya.

3.3 MATERIALS AND EQUIPMENT

3.3.1 MATERIALS

The materials used in the formulations are listed in table 2.

Table 2: Table of materials

	Material	**Quantity(gm)**	**Utility**
1.	Cucurbita pepo seeds	1000g	Active ingredient
2.	Corn starch	500g	Binder/Disintegrant
3.	Crosscarmellose	10g	Disintegrant
4.	Polyvinyl pyrolidone (PVP)	100g	Binder/disintegrant
5.	Sucrose	200g	Binder/sweetener
6.	Kaolin	200g	Absorbent
7.	Microcrystalline cellulose	500g	Diluent/Filler
8.	Lactose	500g	Diluent/filler
9.	Sodium lauryl sulphate	100g	Wetting agent
10.	Colloidal silicon dioxide	100g	Glidant
11.	Talc	200g	Aantiadherent
12.	Magnesium stearate	100g	Lubricant

3.3.2 EQUIPMENT/APPARATUS

The equipment used during formulation included the following,

1. Tablet Press (Erweka, electric type, Germany).
2. Disintegration tester machine (Erweka ZT3, GmbH Heusenstamm, Germany).
3. Tablet hardness tester (Scheuniger, electric type, Germany).
4. Friability tester Machine (Erweka, Heusenstamm, type TA3R, Germany).
5. Shimadzu Weighing balance.
6. Vernier calipers.
7. Sieves.

3.4 EXPERIMENTAL SECTION/PRECOMPRESSION STUDIES ON POWDER

3.4.1 Determination of poured bulk density

This was determined by pouring 10g (M) of the seed powder into a 50ml glass measuring cylinder and the bulk volume (Vo) determined. The bulk density (D_b) was then calculated from the relationship shown;

$D_b = M/Vo$

Triplicate determinations were made and the mean value calculated.

3.4.2 Tapped density

This is the ratio of total mass of powder to the tapped volume of the powder. This was done by tapping the 10g of powder sample after the bulk density determination. The powder was tapped to a constant volume and this volume recorded. The following formula was employed to calculate D_t.

$D_t = M/V$

3.4.3 Determination of the Angle of repose

This was determined by using the funnel method. Accurately weighed powder was taken in a funnel and the height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap. The powder was allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated from the following formula;

$\tan \theta = h/r$

Where ϴ = angle of repose, h = height of powder cone formed, r = radius of powder cone formed.

3.4.4. Determination of Hausner ratio (HR)

This is a measure of the interparticulate friction. It was determined by using the following formula;

Hausner ratio = D_t/D_b

Where D_t is tapped density and D_b is poured bulk density.

The ideal range should be 1.2 -1.5.

3.4.5 Compressibility index

This was calculated using the following formula;

Compressibility index (CI)

CI (%) = { $(D_t-D_b)/D_t$ } x 100

3.5 FORMULATION

The process of granulation was undertaken since the powdered pumpkin seed powder displayed poor flow characteristics as well as compressibility as indicated by the results of preformulation studies. Three formulations were prepared using different binders and disintegrants.

Preparation of seed powder from whole raw pumpkin seeds

The dried pumpkin seeds were ground to a fine powder using the Maulinex standard grinder (180W). The obtained powder was sieved through 710um sieve and packed in an air tight plastic container.

Plate 2: Maulinex grinder and seed powder

Preparation of formulations.

Basic formulations of pumpkin seed powder were prepared as follows. Three formulations were prepared. The wet granulation technique was selected due to its convenience in small scale preparations. In previous studies 500ml of pumpkin seed oil have been prepared as capsules. In this study 250mg of powder was arbitrarily selected for incorporation in the tablet. This was because of the complex nature of phytochemicals present in the pumpkin seed. Raw powder rather than the extract was used in order to maintain efficacy. There is no sufficient data currently that specifies the dose of raw powder to be used. The following ingredients having been screened through 710µm sieves separately were mixed together i.e. Pumpkin seed powder, Microcrystalline cellulose and Lactose were added as a fillers, Kaolin as an absorbent since the pumpkin seed powder is oily in nature. Sodium lauryl sulphate was added to increase wettability of tablet since the presence oils would retard wetting ability and hence disintegration of tablets.

The specific disintegrants for the three formulations were as shown in the tables below. In F1 a superdisintegrant crosscarmellose was used. In F2 polyvinyl pyrollidone was used as disintegrant. In F3 starch was used as disintegrant. These were dry mixed in a motar for five minutes and moistened with the appropriate amount of binder solution. In all cases both binders and disintegrants were mixed intragranularly (rowe and sheskey, 2009).

Wet massing of the ingredients was carried out in a motar using a pestle for ten minutes. The homogenous wet mass was then screened through 1700um sieve and oven dried at 50^{o}C for 2hours. Thereafter the dried granules were screened through 710µm sieve in order to generate uniformly sized granules.

The following extragranular excipients were then added to the sized granules, colloidal silicon dioxide and Talc then mixed. Magnesium stearate was then added and mixed with the granules for one minute. The granulate material was then ready for compression into tablets.

Table 3: Batch preparation F1

No.	**Ingredient**	**Quantity (mg)**
1.	*C. pepo* seeds powder	250
2.	Microcrystalline cellulose	50
3.	Lactose	30
4.	Corn starch	40
5.	Crosscarmellose	10
6.	Kaolin	10
7.	Sodium lauryl sulphate	4
8.	Colloidal silicon dioxide	2
9.	Talc	2
10.	Magnesium stearate	2
	Total	400

Table 4: Batch preparation F2

No.	Ingredient	Quantity (mg)
1.	*C. pepo* seeds powder	250
2.	Microcrystalline cellulose	50
3.	Lactose	30
4.	sucrose	40
5.	Polyvinyl pyrollidone	10
6.	Kaolin	10
7.	Sodium lauryl sulphate	4
8.	Colloidal silicon dioxide	2
9.	Talc	2
10.	Magnesium stearate	2
	Total	400

Table 5: Batch preparation F3

No.	Ingredient	Quantity (mg)
1.	*C. pepo* seeds powder	250
2.	Microcrystalline cellulose	50
3.	Lactose	30
4.	Polyvinyl pyrollidone	40
5.	Corn starch	10
6.	Kaolin	10
7.	Sodium lauryl sulphate	4
8.	Colloidal silicon dioxide	2
9.	Talc	2
10.	Magnesium stearate	2
	Total	400

Plate 3: Sized granules F1

Plate 4: Sized granules F2

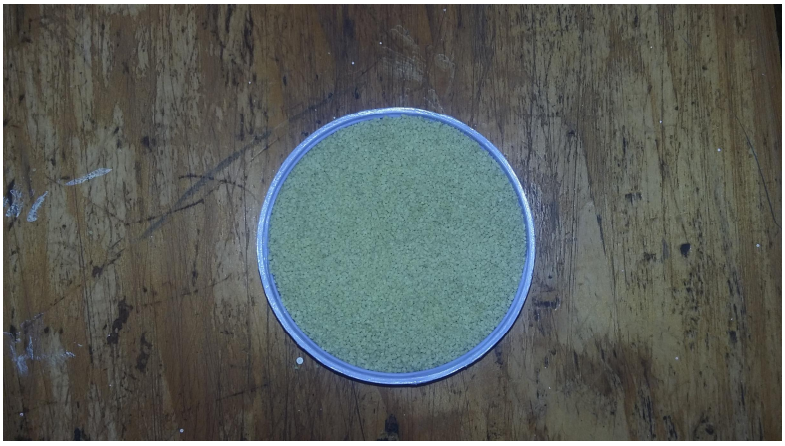
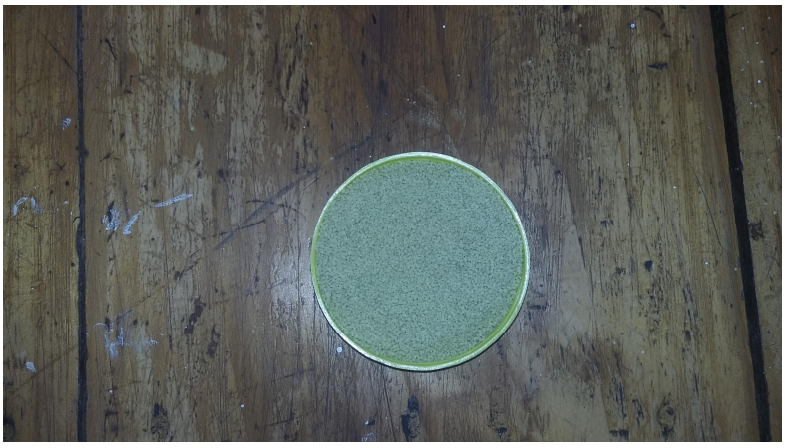


Plate 5: Sized granules F3



COMPRESSION OF TABLETS

The settings of the tableting machine shown in plate 6 were adjusted to give tablets of the required quality. Compression was carried out by taking the above sized granules in a die and compressing them between a set of two punches. Granules were compressed in the single punch tablet compression machine and converted into tablets. The die fill weight was adjusted to give tablets of 400mg weight. The compression force was adjusted until tablets of an appropriate strength were obtained.

Die fill weight = 400mg

Plate 6: Single punch tableting machine

3.6 QUALITY ASSESSMENT/POST COMPRESSION PARAMETERS

3.6.1 General appearance

The macroscopic characteristics of tablets from each formulation were observed i.e. the shape, colour and texture of tablets.

3.6.2 Uniformity of weight

Randomly selected 20 tablets of each formulation were individually weighed and recorded. The average value was calculated and compared to each individual tablet weight.

3.6.3 Hardness test

The hardness of 10 randomly selected tablets of each formulation were determined using the tablet hardness tester shown in plate 7.

Plate 7: Electronic tablet Hardness testing Machine

3.6.4 Friability test

The friability of 20 randomly selected tablets from each formulation was determined. First they were dedusted to remove any loose particles then weighed and the weight recorded as (W_o). They were then placed in a friabilator machine shown in plate 8 below. The machine was then set to rotate at 25rpm for 4 minutes. i.e. 100 revolutions. The tablets were then removed from the friabilator, dedusted using a fine brush and then reweighed and the weight recorded as (W_1).

The percentage weight loss was then calculated and results used to determine whether the tablets passed the friability test.

Plate 8: Friability testing machine

3.6.5 Disintegration test

To study the disintegration profile of the tablets the disintegration test machine shown in plate 9 (Erweka, ZT3, GmbH, Heusenstamm,Germany) was used. 6 tablets from each formulation one at a time were placed in a tube in the machine. The same tube was used for all formulations for all the tests. The machine was then set to run at 31 revolutions per minute and the time taken for each of the tablets to disintegrate and pass through the wire mesh was observed and recorded. The assembly was suspended in a 1000ml beaker filled in with water. The volume of water was such that the wire mesh at its highest point was at least 25mm below the surface of the water, and at its lowest point was at least 25mm above the bottom of the beaker. The water bath was set at a temperature of 37^{o}C +/- 2^{o}C.

Plate 9: Disintegration testing Machine

CHAPTER FOUR: RESULTS AND DISCUSSION

4.1 APPEARANCE

The ground powder from pumpkin seeds was greenish in colour. The results of preformulation studies done on the seed powder are as shown in table 6 below.

The tablets obtained were circular smooth and were greenish in colour. The pictures on plates 10-12 show the tablets obtained from the three batches. Their sizes were ranging between 390-440mg in weight.

Appearance of tablets gives an overall indication of the quality of tablets by simple observation. Mostly specifications for products include size, shape and colour, if these preliminary specifications are not met, then usually there is no need to take them through further testing. Once they comply with the expected appearance then this gives room for further testing to be undertaken. Consistent appearance of tablets is also important for consumer acceptability. The tablets produced were acceptable in appearance and were thus taken through the other quality tests for tablets.

Table 6: Results of Pre-formulation studies of pumpkin seed powder

Property	**Mean (n = 3)**
Bulk density D_b (g/ml)	0.35
Tapped density D_t (g/ml)	0.56
Angle of repose Θ (^{o})	34
Hausners ratio (HR)	1.6
Compressibility index (%)	38

Plate 10: Tablets of Formulation F1

Plate 11: Tablets of formulation F2

Plate12: Tablets of formulation F3

4.2 UNIFORMITY OF WEIGHT

The results from the uniformity of weight test were as shown in table 7.

Table 7: Uniformity of weight test

Formulation	Mean wt. (mg) **n = 20**	Std wt. deviation (%)	Relative std wt deviation (%)	% Deviation of tablet with min wt.	% Deviation of tablet with max wt.	Projected tablet wt. (mg)	% deviation from projected wt.
F1	401	8.52	2.13	2.7	4.7	400	0
F2	409.5	12.34	3.01	4.8	7.4	400	0.02
F3	408	8.33	2.04	2.9	4.3	400	0.02

Based on compedial standards tablets are said to comply with the test for uniformity of weight, if for tablets of average weights greater than 250mg no more than 2 tablets weighed are deviating in weight from the average weight by more than 5%.

Based on these standards, the formulations F1and F3 complied with the test while F2 did not comply. This is because the tablet with maximum weight deviated from the average weight by 7.4%.

This test gives an indication of the uniformity of content within the tablets.

4.3 TABLET HARDNESS TEST

Table 8: Results of tablet hardness test

Formulation	Average hardness (N) n = 10	Max. hardness	Min. hardness	Std. deviation	Relative std. deviation
F1	63.8	72	56	5.3	8.3
F2	55	70	50	5.8	10.5
F3	42.2	48	40	2.9	6.9

This test indicates tablet strength and its resistance to mechanical stress. The harder the tablet is the higher the resistance to friability. Too hard tablets will have a prolonged disintegration time hence the hardness should be just good enough to enable it withstand handling stress and not to affect the disintegration. In house limits of hardness are usually set for each product.

The tablet hardness for this formulation was set at 50N - 120N. In this study F1 had the strongest tablets. A great hardness variation was observed within each formulation and this could be attributed to the fact that the machine was manually operated and hence variation in compression force applied to the successive tablets.

4.4 TABLET FRIABILITY TEST

Table 9: Results of Friability test

Formulation	**%Friability**
F1	0.1
F2	0.2
F3	5.0

Tablets need to have adequate resistance to friability so as to enable them withstand the stresses of transportation from manufacturers, distributors up to the end user the consumer. Highly friable tablets will lose some of the active ingredients during transport and this will result in dose variation. The two formulations F1and F2 showed adequate resistance to friability since the results obtained indicated that the friability was less than 1% which is the stated compedial limit (BP). Formulation F3 had 5% friability and hence did not comply with the specified limits.

4.5 DISINTEGRATION TIME STUDY

Table 10: Results of disintegration time evaluation

Formulation	**Mean disintegration Time (Min) (n = 6)**
F1	14
F2	27
F3	18

For the three formulations F1 displayed the best disintegration time profiles with an average of 14 minutes. F2 showed the longest disintegration time with an average of 27 minutes. This can be attributed to the use of sucrose as binder which is a very strong binder and tablets may harden on storage hence lengthening the disintegration time. F3 displayed slightly longer disintegration time than F1

4.6 COMPARISON OF BINDER USED,MECHANICAL STRENGTH AND FRIABILITY OF TABLETS

Table 11: Comparison of binder, mechanical strength and friability of tablets

Formulation	Binder	Mean mechanical strength(N) (n=10)	% Friability
F1	Starch	63.8	0.1
F2	Sucrose	55	0.2
F3	PVP	42.2	4.9

From the above results it can be deduced that the higher the mechanical strength of tablets the less the friability. This indicates that the F1 formulation had the highest mechanical strength and hence the least friable. Formulation F3 was the weakest formulation in terms of mechanical strength and hence the high friability observed.

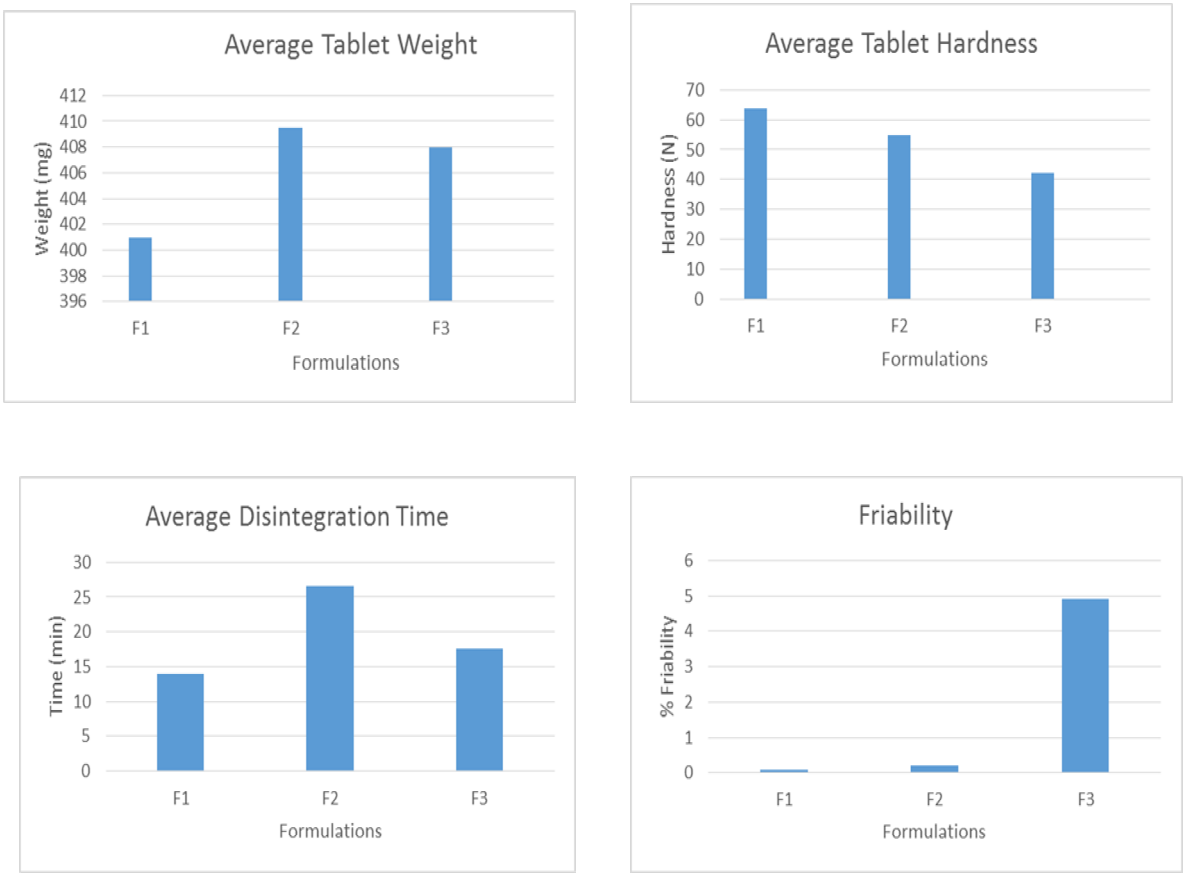
4.7 COMPARISON OF BINDER, DISINTEGRANT USED AND DISINTEGRATION TIME

Table 12: Comparison of Binder, Disintegrant and disintegration time

Formulation	Binder	Disintegrant	Mean disintegration time(min) (n = 6)
F1	Starch	Crosscarmellose	14
F2	Sucrose	PVP	26.6
F3	PVP	Starch	17.6

From the above results it can be deduced that F1 showed the best disintegration time profile. This can be attributed to the presence of crosscarmellose which is a superdisintegrant. The formulation F2 produced tablets with the longest disintegration time. This can be attributed to the use of sucrose which is a very strong binder and hence could have slowed the disintegration. Formulation F3 had a slightly prolonged disintegration time than F1. This formulation can be optimized for disintegration.

Figure 1: Graphs showing comparison of tablet weights, Hardness, Friability, and disintegration time in the different formulations



CONCLUSION

It was concluded that formulation F1 prepared using starch as binder and crosscarmellose disintegrant produced the best formulation based on the results obtained from the quality assessment. It displayed good mechanical strength to withstand handling stresses as well as good disintegration profile to facilitate release of active ingredients. Formulation F2 with sucrose as binder and polyvinyl pyrollidone as disintegrant produced tablets with prolonged disintegration time. Formulation F3 which had polyvinyl pyrollidone binder and starch disintegrant produced tablets whose disintegration time was also slightly prolonged. This formulation also failed the friability test. This formulation was incapable of withstanding handling stresses due to the high friability observed.

RECOMMENDATIONS

Before commercial production of *C.pepo* tablets more research should be done to establish the daily dose, efficacy, and potency. More research should also be done to establish any adverse reactions that can arise from its use as well as other drug interactions that may occur.

Additionally, the seed powder could be capsulated as granules to curb the problem of oil expression during the process of tablet compression when high compression pressures are applied.

It is recommended that further studies be undertaken to establish the stability of these tablets on storage under different climatic conditions to ensure that the product will be suitable for use during the recommended shelf life.

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