



**UNIVERSITI PUTRA MALAYSIA**

***DEVELOPMENT OF HERBAL-BASED ORALLY DISINTEGRATING  
TABLETS FROM *Moringa oleifera* Lam. LEAVES***

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By

**MUHAMMAD AZHAR ALI**

**Thesis Submitted to the School of Graduate Studies, Universiti Putra  
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Doctor of Philosophy**

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Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfillment of the requirement for the Degree of Doctor of Philosophy

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**December 2016**

**Chairman : Associate Professor Yus Aniza Binti Yusof, PhD**  
**Faculty : Engineering**

The *Moringa oleifera* Lam. is a plant from the Moringaceae family. There are about 13 species of the Moringaceae family, of which *Moringa oleifera* is the species most widely known. It is native to Hamalian regions of Pakistan, India. *Moringa oleifera* leaves are rich in multivitamins, minerals, carbohydrates, anti-oxidants and amino acids, however, extreme bitter taste has caused its low acceptability. The aim of present study was to convert whole *Moringa* leaves as one of the advanced forms of pharmaceutical dosage such as the orally disintegrating tablet (ODT). In this purpose, *Moringa* leaves were dried under six different drying conditions as to study the effect of sunlight, drying duration and temperature on vitamins concentration and colour quality. Oven 50 °C drying treatment was found to be optimum in terms of best curve fitting of moisture ratio models, vitamins preservation and colour quality. The dried leaves were ground and the effect of moisture contents, particles shape and size on physical and flow properties of *Moringa* leaves powder were analysed using Box-Behnken technique. *Moringa* leaves powder prepared with a hammer mill having 5% moisture contents and 50 µm particles were selected as the optimum on the basis of flowability standards. A correlation ( $CoI = 0.26CI - 5.47$ ) was established between conventional (Carr Index) and advanced (Cohesion Index) methods for measuring flowability of powders. Banana powder was used as natural superdisintegrant which is one of the main excipient in ODT. The banana powder was prepared using convection oven at 70 °C of 4 mm slice thickness. A comprehensive comparison of prepared banana powder with one of the most commonly used synthetic superdisintegrant, AcDiSol was also done to study its flowability, hardness and disintegration characteristics. Banana powder has superior disintegration properties than AcDiSol but lower in tensile strength. In present formulation, banana

powder acts not only as superdisintegrant but also as a flavouring and nutritious agent. The excipients, such as microcrystalline cellulose (MCC), mannitol, aspartame and vanilla were selected as binder, sweeteners and flavouring agents on the basis of their flowability, hardness and taste masking properties. Simplex Lattice Design of Design of Expert® 8.0 software was used to formulate mixtures of Moringa orally disintegrating tablets. Formulation contained Moringa leaves powder (40%), banana powder (10%), MCC (20%), mannitol (20%), aspartame (5%) and vanilla powder (5%) was selected as an optimum on the basis of Food and Drug Administration (FDA) and The International Pharmacopoeia standards for orally disintegrating tablets. The optimum formulation has hardness, disintegration time and friability of 30.15 N, 50 sec and 0.89%, respectively. The dissolution of formulated tablets was tested in distilled water and simulated saliva using dissolution models to study the dissolution behaviour of tablets when mixed with water and swallowed in the mouth. Korsmeyer-Peppas model described best the dissolution behaviour of Moringa Orally Disintegrating Tablet (MODT). The Korsmeyer  $n$  value of optimum MODT was 1.128 in distilled water which shows rapid disintegration of formulated tablets. The optimum MODT was found not very stable as it gained 5%-6% weight and hardness was also reduced 85%-100% at 75% relative humidity levels. The acute and sub-acute toxicity of optimum formulation were tested on rabbits and found absolutely safe as no damage was observed in liver and kidney cells of rabbits treated with the highest dosage rate of 250 mg/kg body weight. The total theoretical cost including raw materials and processing of optimum MODT was USD 0.023 which is the lowest for any multivitamins available in the Malaysian market. Five tablets per day of MODT have a moderate amount of minerals, amino acids and can fulfil 100% Recommended Dietary Allowance (RDA) of vitamin A (0.6 mg/day) for adolescence.

The present research work provides a fundamental understanding of tableting characteristics of any herb and medicinal plant leaves powder in their pure form. It is the first report of a herbal based orally disintegrating tablet of any herbal and leaves powder of medicinal plant in combination with fruit powder.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia  
sebagai memenuhi keperluan untuk Ijazah Doktor Falsafah

**PEMBANGUNAN HERBA-BASED SECARA LISAN BERPECAH BELAH  
TABLET DARI *Moringa oleifera* Lam. DAUN**

Oleh

**MUHAMMAD AZHAR ALI**

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*Moringa oleifera* Lam. adalah tumbuhan yang berasal daripada keluarga Moringaceae. Terdapat kira-kira 13 spesies keluarga Moringaceae, di mana *Moringa oleifera* adalah spesies yang paling terkenal. Ia berasal dari kawasan Hamalian daripada Pakistan, India. Daun *Moringa oleifera* kaya dengan multivitamin, mineral, karbohidrat, anti-oksida dan asid amino, bagaimanapun, rasa pahitnya yang melampau telah menyebabkan ia mendapat penerimaan yang rendah. Tujuan kajian ini adalah untuk menukar keseluruhan daun Moringa sebagai salah satu bentuk dos farmaseutikal yang maju seperti pil perpecahan unggul (ODT). Dalam kajian ini, daun Moringa telah dikeringkan menggunakan enam jenis pengeringan yang berbeza bagi mengkaji kesan cahaya matahari, tempoh pengeringan dan suhu terhadap kepekatan vitamin dan kualiti warna. Rawatan pengeringan ketuhar pada 50 °C didapati optimum dari segi model lengkung sesuai terbaik nisbah kelembapan, vitamin pemeliharaan dan kualiti warna. Daun-daun kering tersebut dikisar dan kesan kandungan kelembapan, saiz dan bentuk zarah pada sifat-sifat fizikal dan aliran serbuk daun Moringa dianalisis dengan menggunakan teknik Box Behnken. Serbuk daun Moringa yang disediakan menggunakan tukul kilang yang mempunyai 5% kandungan kelembapan dan 50 mikron zarah telah dipilih sebagai nilai optimum berdasarkan piawaian kebolehaliran. Korelasi ( $CoI = 0.26CI - 5.47$ ) telah dibina antara kaedah konvensional (Indeks Carr) dan maju (Indeks perpaduan) untuk mengira kebolehaliran serbuk. Serbuk pisang telah digunakan sebagai bahan perpecahan unggul semula jadi yang merupakan salah satu daripada eksipien utama di ODT. Serbuk pisang telah disediakan dengan menggunakan ketuhar perolakan pada suhu 70 °C dan ketebalan keping 4 mm. Perbandingan menyeluruh serbuk pisang dengan salah satu daripada perpecahan unggul sintetik yang paling biasa

digunakan, AcDiSol juga telah dilakukan untuk mengkaji ciri-ciri kebolehaliran, kekerasan dan perpecahan. Serbuk pisang mempunyai ciri-ciri pecahan unggul daripada AcDiSol tetapi lebih rendah dalam kekuatan tegangan. Dalam penggubalan formulasi ini, serbuk pisang bukan sahaja bertindak sebagai perpecahan unggul tetapi juga sebagai perasa dan ejen berkhasiat. Eksiipien, seperti microcrystalline cellulose (MCC), mannitol, aspartame dan vanila telah dipilih sebagai pengikat, pemanis dan ejen perasa atas dasar kebolehaliran mereka, kekerasan dan sifat rasa pelekat. Simplex kekisi Reka bentuk perisian Expert® 8.0 telah digunakan untuk merumuskan campuran pil Moringa mudah larut. Formulasi yang terkandung pada serbuk daun Moringa (40%), serbuk pisang (10%), MCC (20%), mannitol (20%), aspartame (5%) dan serbuk vanila (5%) telah dipilih sebagai optimum atas dasar Pentadbiran makanan dan Dadah (FDA) dan piawaian Antarabangsa farmakope untuk pil perpecahan unggul. Penggubalan optimum mempunyai kekerasan, masa kehancuran dan kerapuhan masing-masing pada 30.15 N, 50 saat dan 0.89%. Pembubaran pil formulasi telah diuji di dalam air suling dan simulasi air liur menggunakan model pembubaran untuk mengkaji tingkah laku pembubaran pil apabila dicampur dengan air dan ditelan dalam mulut. Model Korsmeyer-Peppas menggambarkan tingkah laku terbaik bagi pembubaran pil perpecahan unggul Moringa (MODT). Nilai Korsmyer-Peppas  $n$  bagi optimum MODT adalah 1.128 dalam air suling yang menunjukkan perpecahan pesat pil formulasi. Optimum MODT optimum didapati tidak berapa stabil kerana pertambahan berat sebanyak 5%-6% dan kekerasan juga berkurang daripada 85% -100% kepada 75% tahap kelembapan relatif. Ketoksikan akut dan sub-akut penggubalan optimum telah diuji pada arnab dan mendapati ia benar-benar selamat kerana tidak ada kerosakan diperhatikan dalam sel-sel hati dan buah pinggang arnab yang dirawat dengan pada kadar dos berat badan tertinggi 250 mg/kg. Jumlah kos teori termasuk bahan-bahan mentah dan pemprosesan optimum MODT adalah USD 0.023 dan ia adalah yang paling rendah bagi mana-mana multivitamin yang terdapat di pasaran Malaysia. Lima biji pil MODT sehari mempunyai jumlah mineral dan asid amino yang sederhana dan dapat memenuhi 100% Recommended Dietary Allowance (RDA) vitamin A (0.6 mg/hari) bagi remaja.

Kerja-kerja penyelidikan semasa ini memberikan asas kefahaman mengenai ciri-ciri sebarang pil herba dan serbuk daun tumbuhan ubatan dalam bentuk tulen. Ia adalah pil perpecahan unggul berasaskan herba yang pertama daripada serbuk herba dan daun tumbuhan ubatan dengan kombinasi serbuk buah-buahan.

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**Muhammad Azhar Ali**



I certify that a Thesis Examination Committee has met on 16 December 2016 to conduct the final examination of Muhammad Azhar Ali on his thesis entitled "Development of Herbal-Based Orally Disintegrating Tablets from *Moringa oleifera* Lam. Leaves" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Doctor of Philosophy.

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## LIST OF ABBREVIATIONS

μL	Micro Liter
μm	Micrometer
AIC	Akaike Information Criterion
ALT	Alanine Aminotransferase
API	Active Pharmaceutical Ingredient
ASAE	American Society of Associate Executives
AST	Aspartate Aminotransferase
BGL	Blood Glucose Level
CI	Carr Index
CDER	Center for Drug Evaluation and Research
CIE	International Commission on Illumination
CoI	Cohesion Index
D <sub>50</sub>	Median Diameter
DNA	Deoxyribonucleic Acid
DoE	Design of Expert
DPX	Dibutyl Phthalate and Xylene
DR	Drying Rate
DT	Drying Time
EUP	European Pharmacopoeia
FBS	Fasting Blood Sugar
FDA	Food and Drug Administration
FAD	Flavin Adenine Dinucleotide
FMN	Flavin Mononucleotide
FSR	Force-Sensitive Resistor
HR	Hausner Ratio
HCl	Hydrochloric acid
HDRA	Henry Doubleday Research Association
HIV	Human Immune Deficiency Virus
HPLC	High Performance Liquid Chromatography

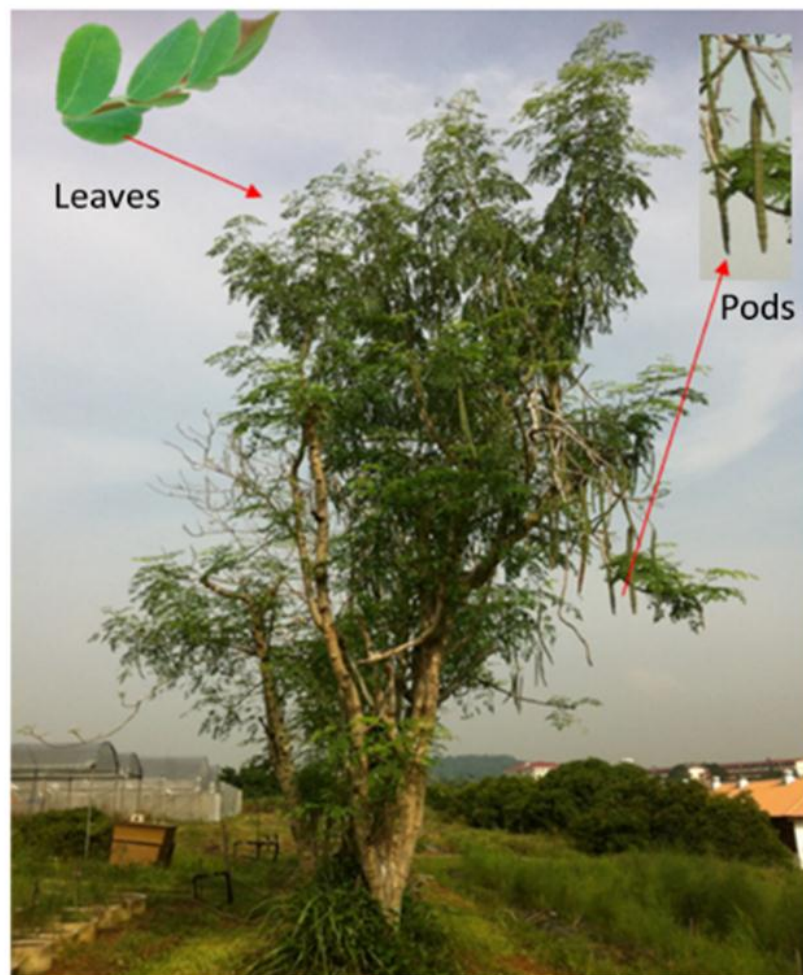
IDRG	International Development Resource Group
kN	Kilo Newton
LCD	Liquid Crystal Display
LD <sub>50</sub>	Lethal Dose
MCC	Microcrystalline Cellulose
mg	Milligram
mL	Milliliter
MLP	Moringa Leaves Powder
MODTs	Moringa Orally Disintegrating Tablets
MPa	Mega Pascal
MR	Moisture Ratio
ODTs	Orally Disintegrating Tablets
OGTT	Oral Glucose Tolerance Test
PFA	Powder Flow Analyser
psi	Pounds Per Square Inch
R <sup>2</sup>	Coefficient of Determination
RBS	Random Blood Sugar
RDA	Recommended Dietary Allowance
RM	Malaysian Ringgit
rpm	Revolution per minute
RMSE	Root Mean Square Error
sec	Seconds
UDU	Uniformity of Dosage Unit
USD	United State Dollar
UV	Ultra violet
X <sup>2</sup>	Reduced Chi Square

## CHAPTER 1

### INTRODUCTION

#### 1.1 *Moringa Oleifera* Tree

The *Moringa oleifera* Lam. tree (Figure 1.1) commonly referred as drumstick tree, miracle tree, tree for life and mother's best friend (Gopalakrishnan *et al.*, 2016) is a plant from the Moringaceae family.



**Figure 1.1 : A 10 years (approximately) old *Moringa oleifera* trees planted at Universiti Putra Malaysia, Serdang, Selangor, Malaysia.**



**Figure 1.2 : Natural growing of Moringa tree (green) and malnutrition (red) regions in World map (Anonymous, 2015a).**

It is native to Pakistan and India and naturalised tropic and sub-tropic regions of the World as shown in Figure 1.2. As the pods are shaped like drum sticks, it is also called drumstick tree. Its roots taste like horseradish, hence also called horseradish tree (Little and Wadsworth, 1964; Morton, 1991). Moringa is a small, fast-growing evergreen tree that usually grows up to 8-10 m in height (Fuglie, 2005). It is a fast growing tree that usually grows up to 10 m height, with grey thick bark and a thin crown. The tree requires an average annual rainfall ranging between 250-3000 mm and survives in a temperature range of 25 to 40 °C which makes it suitable for tropical regions (HDRA, 2002; Ramachandran *et al.*, 1980). Moringa has different names in different languages like Lemungai or Murungai in Malay, Sohanjna in Urdu, Sahijna in Hindi, Maranga calalu in Spanish, Horseradish tree in English, Kelor in Bali, Kaanaeng-doeng in Thai and Saisam in Arabic. It has valued mainly for its edible fruits, flowers, roots, seeds and most importantly leaves in traditional medicine throughout its native and introduced (Figure 1.2) ranges (Lim, 2012). The leaves of Moringa are green in colour and elliptical in shape about 1-2 cm in length (Sharma and Pracheta, 2011). Moreover, being a good source of multivitamins, micro-macro minerals, antioxidants, fatty acids, phenolics and all essential amino acids Moringa leaves have been used in traditional medicines for centuries (Anwar *et al.*, 2007; Fahey, 2005). Moringa leaves also have medicinal properties and various studies conducted on their medicinal usage such as being antioxidant, anticancer, antiviral, cardio-protective, anti-inflammatory, anti-asthmatic and others (Lim, 2012).

### 1.1.1 Nutritional Facts of Moringa Leaves

Scientists who are doing research on Moringa tree reported that Moringa leaves have potential to save the lives of millions of people on our planet as it was estimated that almost 300 diseases can be treated with different parts of Moringa tree. Moringa leaves contain almost 90 nutrients, 18 amino acids and different antioxidants (Fuglie, 2005). There are many claims regarding nutritional facts of dried Moringa leaves, such as 17 times more calcium than cow's milk, 8.8 times more iron than fillet beef, 14 times more potassium than banana, 8 times more vitamin A than carrot and  $\frac{1}{2}$  times vitamin C than orange (Barta, 2011; Fuglie, 2005). There was wide variation in data related to nutrient contents of Moringa leaves. This variation in data was due to agro-climatic conditions, analytical methodology, different stages of leaves maturity and drying method (Makkar and Becker, 1996). So, maximum and minimum range of all nutrients reported in the literature were reviewed and listed in Table 1.1. In the case of vitamins there is only a single source available in which researcher used only shade drying treatment to dry African ecotype Moringa leaves.



**Table 1.1 : Nutrients range of Moringa leaves reported in different studies.**

Nutrients	Units	Value (Range)	References
Protein	g/100g	16-32	Arbeit (2013)
Carbohydrates	g/100g	28-45	
Fat	g/100g	9-22	Moyo <i>et al.</i> (2011) Yaméogo <i>et al.</i> (2011)
Calcium	mg/100g	1088-3512	Offor <i>et al.</i> (2014) Mbah <i>et al.</i> (2012)
Potassium	mg/100g	1120-2290	Asante <i>et al.</i> (2014) Satwase <i>et al.</i> (2013)
Iron	mg/100g	33.5-57.6	Joshi and Mehta (2010)
Copper	mg/100g	0.8-0.9	Olagbemide and Alikwe (2014)
Zinc	mg/100g	4.0-6.1	
$\beta$ -carotene	mg/100g	16.3	
Thiamine	mg/100g	2.64	
Riboflavin	mg/100g	20.5	
Niacin	mg/100g	8.2	Price (2007)
Ascorbic acid	mg/100g	17.3	
$\alpha$ -tocopherol	mg/100g	113	
Histidine	g/100g	0.39-1.90	
Isoleucine	g/100g	0.78-2.33	
Leucine	g/100g	1.55-3.60	
Lysine	g/100g	0.95-1.64	Barta (2011)
Methionine	g/100g	0.23-0.95	Moyo <i>et al.</i> (2011) Sena (1998)
Phenylalanine	g/100g	1.05-4.26	Freiberger <i>et al.</i> (1998)
Threonine	g/100g	0.71-4.38	
Tryptophan	g/100g	0.43-0.75	
Valine	g/100g	1.06-3.36	

## 1.2 Processing of Leaves

### 1.2.1 Drying of Leaves

For the preservation of food items, drying is one of the oldest and widely used methods all over the World. Drying results in altering food properties including colour, aroma, texture, nutritional value and physical appearance. Conditions of drying have a great influence on quality attributes of the dried product. High drying temperature reduces the drying time, but at the same time compromises the quality of the product, may damage the surface and consumes a higher amount of energy. On the other hand, mild drying conditions using lower ranges of temperature may result in improved quality of the product, but reduces the drying rate thus drying period is prolonged (Kumar *et al.*, 2014). There are different conventional and advanced drying techniques being used in field and industry. Conventional methods such as shade, sun and oven drying are used in developing countries. However, advanced methods like microwave and freeze, vacuum and spray drying are commonly used in developed countries. Each method has its own advantages and disadvantages as shade drying at room temperature can conserve nutrients but leads to contamination from surrounding environment such as dust particles, insects and rodents. In sun drying, duration of exposure is less but ultra violet radiations cause destruction of nutrients. The oven drying method is used as standard laboratory method to determine the effect of varying temperatures on product quality in terms of nutrient. Microwave drying is used for rapid drying but very high temperature may burn the heat labile nutrients. Freeze and spray dryings are the advanced methods and nowadays commonly used in industries for heat sensitive food products. Freeze drying method considered to the lowest nutrients loss but it is a very expensive method which limits its applications. While, in spray drying, dry powder is obtained from a liquid composition which changes the biochemistry of product.

### 1.2.2 Powder Formation

After drying, powder formation is the next step in food processing and pharmaceutical industries. Powder formation mechanisms such as dry, hammer and cutter mills commonly used in food industry. Particle size and particle shape are important physical properties of food powders as they have an effect on product performance, bulk properties, flowability, stability, compactability, dissolution and appearance of the end product. Very fine particles having poor flowability can create problems during handling and storage of pharmaceutical powders but having high dissolution rate and vice versa. The flowability of powders can be characterised according to Carr Index (Carr, 1965), Hausner Ratio (Hausner, 1967), Angle of Repose and Cohesion Index (PFA, 2015).

### 1.2.3 Tablet Formulation and Evaluation

Over the past few decades, orally disintegrating tablets (ODTs) have gained much consideration as an ideal substitute to conventional oral dosage forms such as capsules and tablets. The United State Food and Drug Administration Center for Drug Evaluation and Research (CDER) defines the ODT as A solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue (FDA, 2009). The European Pharmacopoeia however, defines a similar term, orodisperse, as a tablet that can be placed in the mouth where it disperses rapidly before swallowing (Sastry *et al.*, 2000). Recent market studies indicate that more than half of the patient population prefers ODTs to other dosage forms and most consumers would ask their doctors for ODTs (Brown, 2003). These responses may, in part, be attributed to knowing ODT advantages such as ease of administration, ease of swallowing, pleasant taste, and the availability of several flavours (Behnke *et al.*, 2003). Orally disintegrating tablets offer all the advantages of conventional dosage form (capsules and tablets) along with following special considerations which include;

- i) As ODT is unit solid dosage form which provides easy manufacturing, small packaging size, better compliance, good stability and precise dosing (Seager, 1998; Habib *et al.*, 2000; Brown, 2003).
- ii) There is no threat of obstruction of this dosage form, which is favorable for travelling patients who may not have access to water.
- iii) Easy to administer in children, elderly, and institutionalised patients (especially psychiatric and mentally retarded patient). Rapid disintegration of the tablet is followed by its fast dissolution and prompt absorption which provide quick onset of action (Badgujar and Mundada, 2011; Dobetti, 2003). In addition, rapid disintegration of tablets may cause rapid dissolution and absorption and thus may cause the medicine to show its effect rapidly (Behnke *et al.*, 2003).
- iv) Flavours and sweeteners in ODTs change the bitter pills into good mouth feel.
- v) Orally disintegrating tablets are preferred especially by children and elderly people as well as the patients who wish to take their medicine at any time comfortably (Sastry *et al.*, 2000; Bandari *et al.*, 2008).
- vi) Absorption of the tablet in mouth avoids liver metabolism, which reduces the dose and increases the amount of active drug in the body (Clarke *et al.*, 2003).

Although Moringa leaves are available in the form of Moringa tea and conventional dosage in some countries but most of the heat labile vitamins (water soluble vitamins) are evaporated at high temperature (Akah and Onweluzo, 2014) of water in case of Moringa tea. Conventional dosage (oral tablet and capsule) undergo a large first pass effect (gastric absorption and liver metabolism). Drug dissolution and absorption, as well as the onset of clinical effect and drug bioavailability (concentration of active drug in the blood) of ODTs may be significantly greater than those observed from conventional dosage forms.

### 1.3 Problem Statement and Objectives

Herbs and leaves of medicinal plants contain rich amount of nutrients and are being used to cure many diseases from centuries. According to World Health Organization, approximately two-thirds of World's population today still relies on herbal medication as component of their primary healthcare (WHO, 2010). After the invention of pharmaceutical dosages like a tablet, capsules and other forms, the use of herbs and medicinal plant leaves in their pure form became limited due to inadequate information about the composition of constituents, inaccurate dosage rate, the toxic effect of pesticides, and conventional drying techniques. Herbal based medications need a scientific evaluation of their pharmacological standards and safety that can be determined using pharmacogenomics technology. With increasing tendencies for the use of naturally derived substances throughout the world, there is a need to conduct pragmatic and explanatory studies considering complementary for acquiring a reliable data for health caregiver as well as for the patient and not to believe in millenarian beliefs and myths. While herbal medicine can potentially contribute to the advancement of healthcare, many major challenges must be overcome prior to the successful integration of herbal medication remedies into mainstream medicine.

Fresh Moringa leaves contained 75% moisture content which make them highly pericable. After drying the taste of Moringa leaves become extremely bitter which is very difficult to swallow. If convert these dried leaves into powder form for further processing like convert into tablet. Powder shows high cohesion and caking strength. Due to low bulk density the nature of powder is very lose and fluffy which make it difficult to process in tablet forming and capsule filling machines because good flowability of powders is the basic requirement of tableting manufacturing process. The hardness and tensile strength of tablets made by Moringa leaves powder also have very less due to which tablets are not very stable during handling and shiping processes. In addition, Moringa leaves also have very poor dissolution in liquid mediums due to very low bulk density, the particles are flot on the surface of liquid medium rather dissolve. The above mentioned problems

are not only associated with only Moringa leaves powder these a very common with all other herbal powders. Therefore, the aim of present study is find a solution which can overcome all above mentioned problems in an economical way.

Additionally, to establish credibility for herbal use in the modern settings, scientific-based studies must be transformed into evidence-based claims. Once these issues are resolved, the prospect exists for the widespread use of herbal medicine as a safe, effective, and affordable form of healthcare.

Therefore, a comprehensive study was planned to introduce herbs and medicinal plant leaves in a more accurate, safe, effective, affordable and readily available form which can compete and fulfill standard parameters described by Food and Drug Administration (FDA) and The International Pharmacopoeia (Ph. Int.) for pharmaceutical dosages. In this purpose, *Moringa oleifera* leaves were selected and effort was made to convert these precious leaves into readily available, acceptable and affordable for all age group of peoples without changing their chemistry (in pure form) such as orally disintegrating tablets.

Therefore, the present study was planned to investigate the use of *Moringa oleifera* leaves in a readily available that is acceptable and affordable to all regions and age groups of people such as tablets (Orally Disintegrating Tablets), in terms of raising the missing vitamins levels.

The objectives of study are:

- i) To determine the drying behaviour, colour quality and nutritional facts of *Moringa oleifera* leaves and banana slices with different drying treatments.
- ii) To evaluate the physical (densities, particles size and shape) and flow (cohesion index and mean caking strength) properties of whole Moringa leaves powder and excipients used in the formulation of Moringa orally disintegrating tablets.
- iii) To develop, formulate and evaluate the Moringa orally disintegrating tablets by direct compression method using different concentrations of diluent, superdisintegrant and sweetener to meet standard parameters.
- iv) To assess the feasibility, stability and toxicological effects of optimum formulated Moringa orally disintegrating tablets.

#### **1.4 Scope of Study**

This study focuses on tableting of Moringa leaves according to the standard parameters described by FDA and International Pharmacopeia for orally disintegrating tablets. The fresh Moringa leaves contained 75% moisture content and bitter in taste. The taste of these leaves become extremely bitter after drying and many vitamins were also lost during conventional (shade and sunlight) drying methods. The powder of Moringa leaves also shown poor flowability which make it difficult to convert into tablet in pure form.

The scope of present research work is illustrated in Figure 1.3.

#### **1.5 Research Hypothesis**

After reviewing the problems related to processing of herbal and medicinal plant leaves in previous literature, the following hypotheses are established.

- i) The standerdisation of herbal and medicinal plant leaves powder can be done according to the parameters described by FDA and International Pharmacopeia.
- ii) Banana powder has the abilities to act as natural superdisintegrant like other synthetic superdisintegrants.

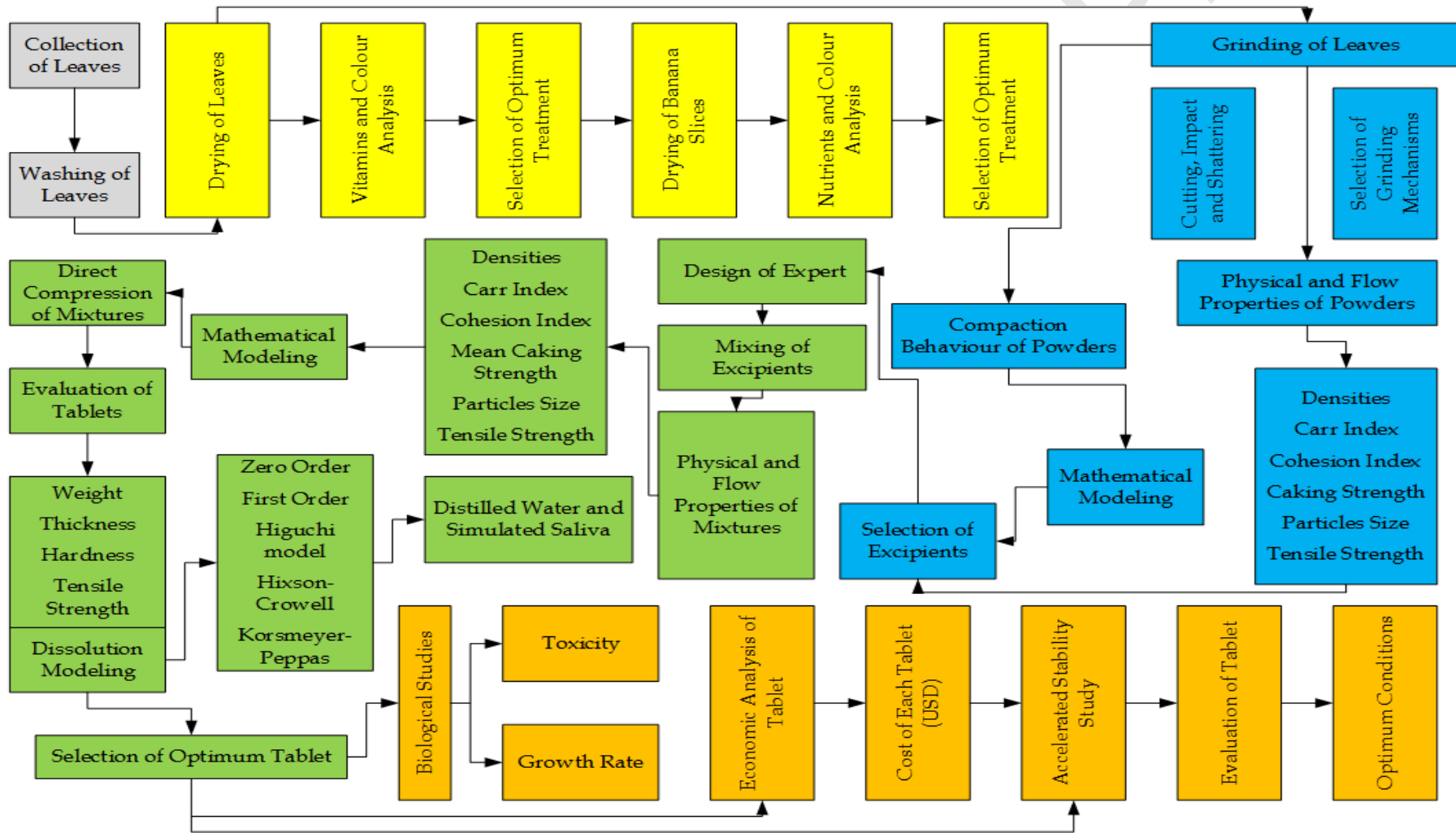


Figure 1.3 : Flow chart for the plan of study.

## 1.6 Outline of the Thesis

**Chapter 1** A comprehensive introduction of *Moringa oleifera* tree, its usage and nutritional facts. Different drying technologies used for leaves drying, conventional and advanced physical and flow properties determination techniques, orally disintegrating tablets advantages and tablet evaluation was given in this chapter. End of this chapter clearly states the problem statement, objectives, hypothesis and plan of study along with an outline of the thesis.

**Chapter 2** Detailed literature is discussed in this chapter in order to obtain sufficient information for experimental design. The drying technologies for leaves, powder flow properties with one of the advanced tool; powder flow analyser, excipients used in the formulation of orally disintegrating tablets, standard parameters for the evaluation of orally disintegrating tablets and biological studies of a drug were reviewed in detail.

**Chapter 3** Presented the details of materials and methods used in drying, empirical modelling, colour analysis and vitamins analysis of fresh and dried Moringa leaves and banana slices. This chapter also concluded the optimum drying treatments for Moringa leaves and banana slices in terms of colour quality and vitamins preservation.

**Chapter 4** Presented the different grinding mechanisms in investigating the effect of particles shape on the flowability of powders. Conventional and advanced methods for measuring physical and flow properties of powders were employed. A correlation between conventional and advanced methods of the flowability measurement was also presented in this chapter. This chapter also disclosed the compaction behaviour using mathematical modelling of whole Moringa leaves powder and all excipients used in the formulation.

**Chapter 5** Explained the direct compression method to make Moringa leaves orally disintegrating tablets and also reported the methodology of tablet evaluation on the basis of parameters set by Food and Drug Administration. The Design of Expert 8.0 ® (DoE) software was used to formulate different excipients at a minimum and maximum level. In this chapter the pre and post compression behaviour of formulated mixtures were determined using standard flowability scales (Carr Index and Cohesion Index) and mathematical modelling. The evaluation of formulated tablets was made according to the standards of Food and Drug Administration and International Pharmacopoeia for orally disintegrating tablets.



**Chapter 6** Determined the stability of optimum formulated Moringa leaves ODTs. The toxic effect of optimum MODT on liver and kidney cells of rabbits, the economic feasibility and final nutritional facts of the optimum tablets in terms of percent recommended daily allowance were examined.

**Chapter 7** A brief conclusion, a summary of experimental results, and future recommendations are stated in this chapter.



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