UNIVERSITI PUTRA MALAYSIA

COMPRESSIBILITY CHARACTERISTICS OF EUCHEUMA COTTONII L. POWDER PREPARED USING MICROCRYSTALLINE CELLULOSE AND KAPPA-CARAGEENAN AS BINDERS

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ZAFIRAH BINTI ZAINAL ABIDIN

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By

ZAFIRAH BINTI ZAINAL ABIDIN

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ZAFIRAH BINTI ZAINAL ABIDIN

December 2011

Chairman: Associate Proffessor Yus Aniza Yusof, PhD

Faculty: Engineering

This thesis presents the study of compressibility characteristics of *Eucheuma cottonii* powder prepared with different binders and methods of compression. *Eucheuma cottonii* is red seaweed that has been cultivated in many tropical countries including Malaysia. This study consists of two different tabletting processes which were tabletting of *Eucheuma cottonii* with microcrystalline cellulose as a binder using direct compression method and the tabletting of *Eucheuma cottonii* with kappa-carrageenan as a binder using a modified wet granulation method. Seaweed has shown potential as anti-obesity, hypocholesterol, antioxidant and organ protective properties on cardiovascular health. A commercial universal testing machine with a 13-mm cylindrical stainless steel uniaxial die has been used in this study for the compression of powder. Seven different compositions of binder ranging from 0% (w/w) to 100% (w/w) with two different amounts of feed powders, 0.5g and 1.0g have been prepared. Pressures within the range of 7.5 to 74 MPa have been used during the compression process. A constant

compression speed of 5 mm min^{-1} has been applied throughout the compression process. Effect of different amounts of feed powders and composition of binders on compression characteristics has been studied. Relationship such as volume-pressure, density-pressure, ejection force-force and tensile strength-pressure were represented in order to study the compression characteristics of *Eucheuma cottonii*. To understand the result further, three compression equations were used, Kawakita and Lüdde, Heckel and Walker. The best tablet formulation for both tabletting processes was determined. For tabletting of *Eucheuma cottonii* with microcrystalline cellulose, it has been determined that tablet with 70% microcrystalline cellulose as a binder is the best formulation whereas for the tabletting of *Eucheuma cottonii* with kappa-carrageenan as a binder, tablet which the composition containing 10% kappa-carrageenan as a binder has been the best formulation. Based on this approach, a better understanding of the compressibility characteristics of *Eucheuma cottonii* is obtained which is essential for the enhancement of the tabletting industry in Malaysia.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Master Sains

SIFAT KEBOLEHMAMPATAN SERBUK *EUCHEUMA COTTONII L.* DISEDIAKAN MENGGUNAKAN MICROCRYSTALLINE CELLULOSE DAN KAPPA-CARRAGEENAN SEBAGAI PENGIKAT

Oleh

ZAFIRAH BINTI ZAINAL ABIDIN

Disember 2011

Pengerusi : Profesor Madya Yus Aniza Yusof, PhD

Fakulti : Kejuruteraan

Tesis ini membentangkan kajian tentang sifat-sifat mampatan bagi serbuk *Eucheuma cottonii* di bawah pengaruh pengikat yang berbeza dan kaedah mampatan. *Eucheuma cottonii* merupakan sejenis rumpai laut merah yang telah dibiakkan di kebanyakan negara-negara tropika termasuk Malaysia. Kajian ini meliputi dua kaedah penghasilan tablet yang berbeza iaitu kaedah penghasilan tablet *Eucheuma cottonii* bersama-sama 'microcrystalline cellulose' sebagai pengikat melalui kaedah mampatan terus dan kaedah penghasilan tablet *Eucheuma cottonii* bersama-sama "kappa-carrageenan " sebagai pengikat melalui kaedah penggranulan basah yang telah diubahsuai. Rumpai laut telah menunjukkan potensi sebagai anti- obesiti, 'hypocholesterol', antioksidan dan sifat pelindung organ dalam kesihatan kardiovaskular. Sejenis mesin penguji komersial universal beserta acuan keluli satu arah berdiameter 13 mm telah digunakan di dalam kajian ini bagi tujuan pemampatan serbuk. Tujuh komposisi pengikat yang berbeza di dalam julat 0% (b/b) hingga 100% (b/b) dengan dua jisim serbuk yang berlainan iaitu

0.5 dan 1.0g telah disediakan. Tekanan di dalam julat 7 hingga 74 MPa telah digunakan semasa proses mampatan. Kadar kelajuan mampatan yang malar iaitu 5 mm min^{-1} telah digunakan sepanjang proses mampatan. Kesan jisim serbuk yang berbeza dan komposisi pengikat yang berbeza terhadap sifat-sifat mampatan *Eucheuma cottonii* telah dikaji. Hubungan seperti isipadu-tekanan, ketumpatan–tekanan , daya pengeluaran tablet-tekanan dan kekuatan tegangan tablet-tekanan telah dipersembahkan untuk mengkaji sifat-sifat mampatan *Eucheuma cottonii.* Untuk lebih memahami hasil kajian, melalui tiga persamaan mampatan digunakan iaitu persamaan 'Kawakita and Lüdde', 'Heckel' dan 'Walker'. Formulasi tablet yang melepasi syarat-syarat yang ditetapkan telah dicadangkan bagi tujuan pengkomersialan. Bagi tablet *Eucheuma cottonii* dengan 'microcrystalline cellulose' sebagai pengikat, formulasi yang mengandungi 70% microcrystalline cellulose sebagai pengikat telah dicadangkan manakala bagi tablet *Eucheuma cottonii* dengan kappa-carrageenan sebagai pengikat, formulasi tablet yang mengandungi 10% kappa-carrageenan sebagai pengikat telah dicadangkan. Melalui pendekatan ini, pemahaman tentang sifat-sifat mampatan yang ditunjukkan oleh *Eucheuma cottonii* telah diperolehi yang mana ianya penting untuk mengembangkan lagi industri penghasilan tablet di Malaysia.

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I certified that an examination committee has met on 16th December 2011 to conduct the final examination of Zafirah Binti Zainal Abidin on her Master of Science thesis entitle "Compression Characteristics of *Eucheuma Cottonii* Powder with Microcrystalline Cellulose and Kappa-Carageenan as Binders" in accordance with Universiti Pertanian Malaysia (Higher Degree) Act 1990 and Universiti Pertanian Malaysia (Higher Degree) Regulations 1981. The Committee recommended that candidate be awarded relevant degree. Members of the Examination Committee were as follows:

GANTI

Chairman, PhD
Y. Bhg. Prof. Dr. Russly Abdul Rahman
Faculty of Engineering
Universiti Putra Malaysia
(Chairman)

Examiner 1, PhD
Dr. Rosnita A. Talib
Faculty of Engineering
Universiti Putra Malaysia
(Internal Examiner)

Examiner 2, PhD
Dr. Farah Saleena Taip
Faculty of Engineering
Universiti Putra Malaysia
(Internal Examiner)

External Examiner, PhD
Assoc. Prof. Dr. Ahmad Zuhairi Abdullah
School of Chemical Engineering
Engineering Campus
Universiti Sains Malaysia
(External Examiner)

_____

Prof. Dr. Seow Heng Fong
Professor and Deputy Dean

School of Graduate Studies

Universiti Putra Malaysia

Date:

This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfillment of the requirement for the degree of Master of Science. The members of the Supervisory Committee were as follows:

Yus Aniza Yusof, PhD
Associate Professor
Faculty of Engineering
Universiti Putra Malaysia
(Chairman)

Suhaila Mohamed, PhD
Professor
Institute of Bioscience
Universiti Putra Malaysia
(Member)

Chin Nyuk Ling, PhD
Associate Professor Ir.
Faculty of Engineering
Universiti Putra Malaysia
(Member)

_____

BUJANG KIM HUAT, PhD
Professor and Dean
School of Graduate Studies
Universiti Putra Malaysia

Date:

DECLARATION

I declare that the thesis is my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously, and is not concurrently, submitted for any other degree at Universiti Putra Malaysia or any other institution.

ZAFIRAH BINTI ZAINAL ABIDIN

Date: 16 December 2011

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B	Heckel's intercept	
C	volume reduction	
d	Tablet diameter	[m]
F	Crushing strength or tensile strength	[N]
K	Heckel's slope	[MPa]
m	weight of powder	[g]
σ	Yield Strength, represent as a minimum applied pressure required to deform coherent tablet	[MPa]
σ_t	Tensile strength	[MPa]
P	Applied pressure	[MPa]
P_k	Kawakita and Lüdde's derivative; represent as pressure required to reduce the volume of the powder bed by 50%	[MPa]
P_y	Yield pressure; represent as the ability of the materials to deform plastically under applied pressure	[MPa]
ρ_a	Apparent density	[kg m^{-3}]
ρ_b	Bulk density	[kg m^{-3}]
ρ_{rel}	Relative density	[kg m^{-3}]
ρ_{brel}	Relative bulk density	[kg m^{-3}]

ρ_t	True density	[kg m^{-3}]
ρ_{tap}	Tapped density	[kg m^{-3}]
t	Compact thickness	[m]
V	Volume at applied pressure	[m^3]
V_b	Bulk volume	[m^3]
V_o	Initial volume at zero applied pressure	[m^3]
V_t	True volume	[m^3]
V_R	Relative volume	[m^3]
V_{tap}	Tapped volume	[m^3]
w	weight of sample	[g]
W	Walker's slope; represent as compressibility coefficient	[MPa]

LIST OF ABBREVIATIONS

CI	Carr Index
HR	Hausner Ratio
MCC	Microcrystalline cellulose
κ-carrageenan	Kappa-carrageenan

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CHAPTER 1
INTRODUCTION

1.0 Introduction

This chapter briefs on background of *Eucheuma cottonii* and also its nutritive value and therapeutic properties. The compression process is being introduced. This chapter also reviews on other research done on *Eucheuma cottonii,* limitations of study and objectives of study. The outline of this thesis is presented at the end of the chapter.

1.1 *Eucheuma Cottonii*

1.1.1 Background of *Eucheuma Cottonii*

In many maritime countries, seaweeds have been widely used as a food sources especially in Asia countries like Japan, Korea and China. Apart from that, use of seaweed is also recognized in many other industries that produce cosmetics, fertilizer and also in the industrial gums and chemicals extraction. Moreover, seaweeds also have the potential as a chemical to be used in the medicine (Anonymous, 2011a). Besides the application of seaweed in many industries, it is also shown a positive effect on human health. Studies have shown that seaweeds have anti-obesity, hypocholesterol, antioxidant and organ protective properties on cardiovascular health (Matanjun, 2008). Seaweed can be classified into three major groups which are red, brown and green seaweed (Anonymous, 2011c).

Eucheuma cottonii (Bryceson, 2002; Rönnbäck, et al., 2002) is a species of red seaweed (Rhodophyta) which is cultivated in many tropical countries. In aquaculture industry, this species has been extensively farmed at places like on the reef edge that has a strong wave action (Reine and Trono, 2001). The physical characteristics of *Eucheuma cottonii* are tough, fleshy and firm. The growth of *Eucheuma cottonii* can be up to 2m tall. The colour of *Eucheuma cottonii* is shiny green to yellow orange. The widely known product of *Eucheuma cottonii* is carrageenan.

1.1.2 Nutritive Value Of *Eucheuma Cottonii*

Eucheuma cottonii contains high amount of ash (~ 46.19%) and dietary fibers (~25.05%) and low in lipid content (~ 1.10%) on dry weight (DW) basis (Matanjun, et al., 2009). It also contain macro-minerals like Na, K, Ca and Mg (Matanjun, et al., 2009). The content of polyunsaturated fatty acid in Euc*heuma cottonii* is significant and majority component of it is omega-3 fatty acid (Matanjun, et al., 2009).The crude protein content of *Eucheuma cottonii* is 9.76% dry weight and it also has considerable amount of vitamin C (~35 mg.100 g^{-1}) (Matanjun, et al., 2009). *Eucheuma cottonii* contains ascorbic acid and polyphenols (Fayaz, et al., 2005) and it also has low total phenolic content (Chew, et al., 2008)

1.1.3 Therapeutic Properties of *Eucheuma Cottonii*

Nowadays, synthetic antioxidants is no longer opt by consumer because of the toxicity and carcinogenic effects (Ito, et al., 1986; Safer and Al-Nughamish, 1999). Consequently, antioxidants from natural sources is favored (Kranl, et al., 2005). Pavia and Aberg found (1996) an excellent antioxidant, phloroglucinol phenolics (phlorotannins) (Ragan and Glombitza, 1986) in marine algae. According to Tapiero, et al. (2002), polyphenols containing antioxidants able to shield the tissue of the body from oxidative stress and pathologies such as cancer, coronary heart disease and also inflammation. *Eucheuma cottonii* have been reported to provide various health benefits however its use in food is limited due to its taste. This brings out the idea of producing the *Eucheuma cottonii* in a tablet form. Usually, tablet can be easily swallowed and can be formed into various shapes and sizes.

1.2 Tabletting Process

In pharmaceutical industry, tablet is the most common used dosage form bear to the reason that it is easy to manufacture, it offers convenience of dosing and it is stable compare to liquid and semi-solid presentations. Tablets usually consist of active ingredient and several inert materials, referred as excipients, which is present in satisfactory amounts to accomplish pharmaceutical, nutritive or chemical effect. Excipients can be classified according to their function, which are diluents, binders, binder-diluents, disintegrants, lubricants, glidant and antiadhesive. The mixture of active

ingredients and excipients which is in powder form will be compressed to produce tablet.

Binder is an excipient added into the formulation to increase the ability of powders to form coherent tablets and to improve the mechanical strength of materials as well as to ensure that the tablets are large enough to be easily handled. In order to choose a binder to be added into the formulation of a tablet, one must make sure that the binder must fulfill certain requirements for example it must shows a superior binding functionality and also good powder flowability. Not only that the particle size distribution and its compatibility with other excipients or drugs should also be emphasized (Bolhuis and Chowhan, 1996). Apart from the binder, the parameters used during compression process also influence the overall efficiency of the tabletting such as the effect of pressure, solid loading and compression speed (Sinka, et al., 2009).

Since compression is a complex process, it has led to the majority of fundamental studies has been carried out on single materials (Narayan and Hancock, 2005; Sonnergaard, 2006; Davies, et al., 2007; Odeku and Picker-Freyer, 2007). Nevertheless, since tablets consist of more than one material, the study of the compression properties of mixtures has become an obvious interest (Martinello, et al., 2006; Michrafy, et al., 2009). Excipient for each active ingredient or combination of ingredient in a tablet formulation must be correctly selected in order to achieve the desired response and it is not in practice a simple goal to achieve. The formulator must assure that the correct amount of active ingredients in the right form is delivered at or over the proper time at the proper rate and in the desired location while having its chemical integrity protected

to that point. The influence of the active ingredients and the excipients are worth to be considered to measure their effect on the pharmacological reaction of any tablet system.

1.3 Review of *Eucheuma Cottonii* Research

Generally, all studies on *Eucheuma cottonii* has been on the extraction of carrageenan which is the main cell wall material of *Eucheuma cottonii* and the application of the extracted carrageenan (Rochas, et al., 1989; Montolalu, et al., 2007) . Apart from that, study on advance technology on farming of *Eucheuma cottonii* has been carried out extensively (Ask and Azanza, 2002; Pickering, 2006). In recent years, there has been an increasing interest on therapeutic properties of *Eucheuma cottonii*. A group of researcher from Faculty of Food Science and Technology, Universiti Putra Malaysia has been involved actively on research of nutrient content and health benefits offered by *Eucheuma cottonii* (Matanjun, 2008). Attempt has also been made by them on producing capsule of *Eucheuma cottonii*.

Most of the research done on *Eucheuma cottonii* has been on the chemical and therapeutic properties of it (Chew, et al., 2008; Matanjun, et al., 2009). In spite of this, study on compression characteristics of *Eucheuma cottonii* and the ability of *Eucheuma cottonii* to be compressed into tablet has never been carried out before.

1.4 Scope of study

The research to date has tended to focus only on chemical and therapeutic properties of *Eucheuma cottonii* rather than the mechanical properties of it. There is no attempt yet has ever been made on compression of *Eucheuma cottonii*. For this reason, in this study, *Eucheuma cottonii* powder with different types of binder and method of production were compressed by a unixial die compaction method under the pressure ranging from 7 to 74 MPa using a universal testing machine.

The tablets produced were tested upon its tensile strength, friability and disintegration properties. The tensile strength of pure material should be more than 0.3 MPa which is considered as the minimum strength for oral tablet (Odeku, 2009). For the second requirement, the friability value of the tablet must not be more than 1% (Odeku, 2009) and the last one is through the disintegration analysis (*British Pharmacopoeia*, 1998) which is carried out by modified disintegration test.

1.5 Research Objectives

The main objectives of this thesis are:

i. To determine the potential of Kappa-carrageenan as a natural binder in producing that is cheaper and also has high possibility to replace commercial binder.

ii. To investigate the compression behavior of *Eucheuma cottonii* powder through three commonly used compression models and obtaining an acceptable amount of binder to be added in the formulation of *Eucheuma cottonii* tablets.

1.6 Outline of The Thesis

The introduction chapter introduces the background of the *Eucheuma cottonii* together with the review on its therapeutic properties. The chapter also presents the limitation and the objectives of the study. Apart from that, the significance of research to tabletting industry is also presented in this chapter.

Chapter 2 starts with an introduction of methods commonly used in tablet production in which detail explanation on wet granulation and dry granulation process is included. The compression process and the equation used for the analysis of tabletting process are explained briefly in this chapter. Fundamental of mechanical strength of tablet is discussed as well as description on factors affecting mechanical strength of tablet. The components of tablet followed by the review on used of binder as strength enhancing material are also reviewed.

Chapter 3 describes in detail the experimental design and the methods used in this research. Material properties of powder prior to compression are presented. At the end of this chapter, details on the approach used in choosing the suggested formulation are presented.

Chapter 4 elucidates the effect of the quantity of feed powder and composition of binders and pressure on the compression behavior of *Eucheuma cottonii* and it is explained in two sections which are the relationship of density and volume with pressure and the second one is the tensile strength profile. The mechanical strength properties of

tablet are examined by tensile strength, friability and disintegration of tablet. Several compression equations are used with the intention of validating the previous data. Suggested formulation is given by taking into consideration the mechanical and dissolution property of the tablet.

Summary on all work and findings are exhibited in Chapter 5. Recommendations for future work are also given in this final chapter.

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