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THE PHYSICOCHEMICAL CHARACTERIZATIONS OF THE BINARY MIXTURE OF ACETAMINOPHEN AND SELECTED CHEMICAL CONSTITUENTS OF LABISIA PUMILA BY SOLID DISPERSION TECHNIQUE

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ABSTRACT

Acetaminophen (APAP),the most common drug used widely was blend with selected chemical constituents of *Labisia Pumila* to glance for new phase of interactions leading to new compound phase. These selected chemical constituents of *Labisia Pumila* were divided into five groups; hydroxycinnamic acid, hydroxybenzoic acid, Flavonoids, Ascorbic Acid and Lab A. The interaction obtained from the binary interaction of two solid dispersion techniques; Neat Grinding (NG) and Liquid Assisted Grinding (LAG). The compounds demonstrate different stoichiometry of binary mixture ratio of acetaminophen and selected chemical constituents of *Labisia Pumila* at 1:1 molar ratio, 1:2 molar ratio and 2:1 molar ratio. The interaction estimated using Group Contribution Method (GCM) theoretically and the physicochemical properties were characterized by using Attenuated Total Reflectance Fourier Transform Infrared (ATR-FTIR), Powder X-ray Diffraction (PXRD) and Differential Scanning Calorimetry (DSC) analysis. The GCM calculations gave good interaction strength at range 102.81 MPa$^{1/2}$ – 189.53 MPa$^{1/2}$ for hydroxycinnamic acid group; 115.34 MPa$^{1/2}$ – 208.43 MPa$^{1/2}$ for hydroxybenzoic acid group, 165.36 MPa$^{1/2}$ – 212.93 MPa$^{1/2}$ for flavonoid groups, 203.89 MPa$^{1/2}$ for ascorbic acid and 126.86 MPa$^{1/2}$ for alkenyl compounds and benzoquinone group respectively. ATR-FTIR data analysis showed the majorly peak of –NH group was shifted from 3318.91 cm^{-1} to range 3314 cm^{-1} – 3301 cm^{-1}. While –OH group was shifted from 3108.16 cm^{-1} to ~3068 cm^{-1} – 2400 cm^{-1}. Lastly C=O functional group showed the shifted from 1651 cm^{-1} to range 1648 cm^{-1} – 1753 cm^{-1}. DSC data analysis showed most of the melting temperature thermograms formed new phases at range of 151°C – 170 $^{\circ}$C with difference value of heat of fusion, represent the strength of interaction formed during the changes of phase transformation from solid to liquid phase of binary mixture blends. Meanwhile, in PXRD data analysis, the changes in peak intensity, peak shifted and d-spacing were showed at range of 5° – 50° in the binary mixture blends. The ATR-FTIR, DSC and PXRD results obtained revealed interactions with new phase formed indicated from the peak shifted or new peak phase formation. The physicochemical characterization showed that 1:2 molar ratio of liquid assisted grinding (tetrahydrofuran) was selected as the best stoichiometric for Cinnamic Acid, 1:1 molar ratio of liquid assisted grinding (acetonitrile) selected for p-coumaric acid, 2:1 molar ratio of neat grinding has been selected for caffeic acid, 1:1 molar ratio of liquid assisted grinding (methanol) was selected for chlorogenic acid, molar ratio 2:1 liquid assisted grinding (tetrahydrofuran) has been selected as the best stoichiometry in benzoic acid, 1:1 molar ratio of liquid assisted grinding (tetrahydrofuran) selected as best ratio for salicylic acid, neat grinding 1:2 stoichiometry was chosen for syringic acid. As for flavanols, 2:1 molar ratio of liquid assisted grinding (acetone) was selected as best stoichiometry for naringenin, 1:2 liquid assisted grinding (acetonitrile) selected for quercetin and 2:1 molar ratio of liquid assisted grinding (acetonitrile) has been selected as best stoichiometry for binary mixture of acetaminophen / rutin hydrate. In addition, it was found that 1:2 molar ratio of liquid assisted grinding (acetonitrile) was selected for ascorbic acid and lastly, 1:2 molar ratio of liquid assisted grinding (acetonitrile) was selected as the best stoichiometry for formation of binary mixture between acetaminophen and Lab A.

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TABLE OF CONTENT

CHAPTER ONE
INTRODUCTION

1.1   Research Background

According to World Health Organization (WHO), traditional medicine (TM) can be defined as sum of knowledge, skills and practice based on the theories, beliefs incorporating plant-, animal- and mineral-based medicines and experiences indigenous to different cultures and thus it has been used to maintain health. Several studies have revealed that in some Asian and African countries, it is estimated that 80% of the population living in rural areas uses traditional medicine for primary health care needs, meanwhile in many developed countries, about 70% to 80% of the population has used traditional medicine as adaptations of traditional medicine which are termed as "complementary" or "alternative" medicine (CAM) (Ekor, 2013; WHO, 2008; Ilse, 2007; Bannerman, 1983). Hence, it has conclusively been shown that herbal medicine treatments are the most popular form of traditional medicine used in recent research study.

Herbal medicines consist of four main courses which are herbs, herbal materials, herbal preparations and finished herbal products. These herbal medicines contain active ingredients parts of plants, or other plant materials, or either with combination process. Active ingredients refer to the ingredients of herbal medicines consist of therapeutic activity characterization. Therapeutic activity refers to the successful process of prevention of illness, diagnosis and treatment of physical and mental illnesses; improvement of symptoms of illness as well as beneficial alteration or regulation of the physical and mental status of body. Therefore, in herbal medicines, preparation of these medicines should be standardized to contain a defined amount of active ingredients.

Labisia Pumila (Myrsinaceae), or popularly known as "*Kacip Fatimah*", traditionally used in Malay traditional medicine by many generations of Malay women in the form of decoction as postpartum tonic which can induce and facilitate childbirth, also has been found as popular and global use as functional food and beverage to regain body strength (Ezumi*et al.,* 2007; Burkill, 1935). *Labisia Pumila* is the queen of the herbs and it was listed as one of the high-valued herbs in Entry Point