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CHEMICAL CONSTITUENTS AND BIOLOGICAL ACTIVITIES OF *Artocarpus communis* AND *Artocarpus odoratissimus* LEAVES EXTRACTS

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ABSTRACT

Previous studies revealed that *Artocarpus* species contained several bioactive compounds with potential to provide relief in treatment of diarrhea, wound healing and liver cirrhosis but never been tested for its cytotoxicity properties against liver cell lines to confirm this traditionally medical uses with modern scientific test. Therefore it would be interesting to study the cytotoxicity properties of isolated pure compounds against liver cell line such as Hep-G2 together with other bioassays such as antioxidant and antimicrobial. The dried leaves of *A. communis* and *A. odoratissimus* were extracted using cold extraction in methanol. Various chromatographic methods such as vacuum liquid chromatography, thin layer chromatography and radial chromatography were used to isolate and purify compounds from the methanolic extracts of both plants. Structural elucidation was accomplished using spectroscopic methods such as ultraviolet, infrared, mass spectroscopy, 1D and 2D nuclear magnetic resonance. This study resulted in identifying three flavonoids and three triterpenoids namely squalene (**130**), 1-(2,4-dihydroxyphenyl)-3-[8-hydroxy-2-methyl-2-(4-methyl-3-pentenyl)-2H-1-benzopyran-5-yl]-1-propanone (**9**), 8-(3,6-dimethyl-2-heptenyl)-4',5,7-trihydroxyflavanone (**28**), 2-geranyl-2',3,4,4'-tetrahydroxydihydrochalcone (**11**), stigmasterol (**132**) and *β*-sitosterol (**131**). The methanolic leaves extracts for both *A. communis* and *A. odoratissimus* and some of the isolated pure compounds were tested for its antioxidant and antimicrobial activities. Some of these samples demonstarted interesting results in free radical scavenging activity assay; 2-geranyl-2',3,4,4'-tetrahydroxydihydrochalcone showed the most interesting free radical scavenging activity with IC_{50} value of 5.84 µg/mL as compared to positive control, ascorbic acid with IC_{50} value of 10.24 µg/mL while, 8-geranyl-4',5,7-trihydroxyflavanone is comparable with control as IC_{50} recorded at 12.93 µg/mL. Antimicrobial activities based on MIC and MBC revealed some of the tested compounds exhibited strong inhibition activity against Gram-positive bacteria, *Staphylococcus aureus, Streptococcus pyogenes* and Gram-negative bacteria, *Pseudomonas aeruginosa* and *Escherichia coli* with MIC value between 7.03 to 56.25 µg/mL. Pure compound 2-geranyl-2',3,4,4'-tetrahydroxydihydrochalcone demonstrated the most promising inhibition activity against both Gram-positive with MIC value of 7.03 µg/mL, the same MIC value for positive control, streptomycin sulphate. Meanwhile, 1-(2,4-dihydroxyphenyl)-3-[8-hydroxy-2-methyl-2-(4-methyl-3-pentenyl)-2H-1-benzopyran-5-yl]-1-propanone showed more potent cytotoxic effect on Hep-G2 (IC_{50} = 8 µg/mL) and followed by 2-geranyl-2',3,4,4'-tetra hydroxyldihydrochalcone (IC_{50} = 9 µg/mL). Results from this bioactivity investigation suggested that 1-(2,4-dihydroxyphenyl)-3-[8-hydroxy-2-methyl-2-(4-methyl-3-pentenyl)-2H-1-benzopyran-5-yl]-1-propanone (**9**) and 8-(3,6-dimethyl-2-heptenyl)-4',5,7-trihydroxyflavanone (**28**), together with compound 2-geranyl-2',3,4,4'-tetrahydroxydihydrochalcone (**11**) isolated from *A. communis* may have great potential for further development as cancer chemoprevention agents or food supplements for promoting human health.

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INTRODUCTION

1.1 GENERAL INTRODUCTION

First pharmacologically active compound called morphine which was isolated between 1803 and 1805 which has been discovered from opium poppy *(papaver somniferum)* has become the stimuli in drugs discovery from nature especially in plants. The research expended after the Second World War in 1945 due to high demands for treatment after post war for treatment to moderate and severe pain and substitute for painkiller. Hence, pharmaceutical research broadens and involving microorganisms screening after penicillin which was discovered by Alexander Fleming in 1940. This great discovery triggered advance in pharmaceutical research by introduction of antibiotics which can cure bacteria, fungi and parasites infections. By 20^{th} century, about 80% of drugs are derived from natural products, but in 21th century, new drugs discovery based on natural products were declining up to 50%. This is due to the prevailing paradigm for drug discovery in large pharmaceutical industries and technical limitations in identifying new compounds with desirable activity (Jesse and John, 2009). The reason behind this situation mainly for commercial purpose such as cost effective and time less consumed for larger quantities of production for the pharmaceuticals companies.

However, natural products have tremendous effect in medical industries endlessly and yet providing a dominant role in drug discovery for treating human diseases and becoming prevention methods such as fighting illness, cancer prevention and cure for infectious diseases. Other than that, natural products still often extracted to produce daily supplements and cosmetic products to maintain health due to hectic lifestyle. Moreover, benefits in plants as medication in form of herbs and traditional medicine which has been practiced for a long time in Asian tradition such as Ginseng (*Panax quinquefolius*) and Tongkat Ali (*Eurycoma longifolia*) which can be acquired in their surroundings and easily accessible. Kamal & Mohan (2010) estimated that 80% of the world population still using plants or herb based as a medicine and about two-thirds out of 50,000 of the medicine plants were from natural habitat. Most rural