FRGS GRANT

Deciphering Modulation of Anti-inflammatory and Antioxidative Morindolide on the Crosstalk between MEK1/JNK/NF-kB/iNOS and Nrf2/HO-1 Pathways

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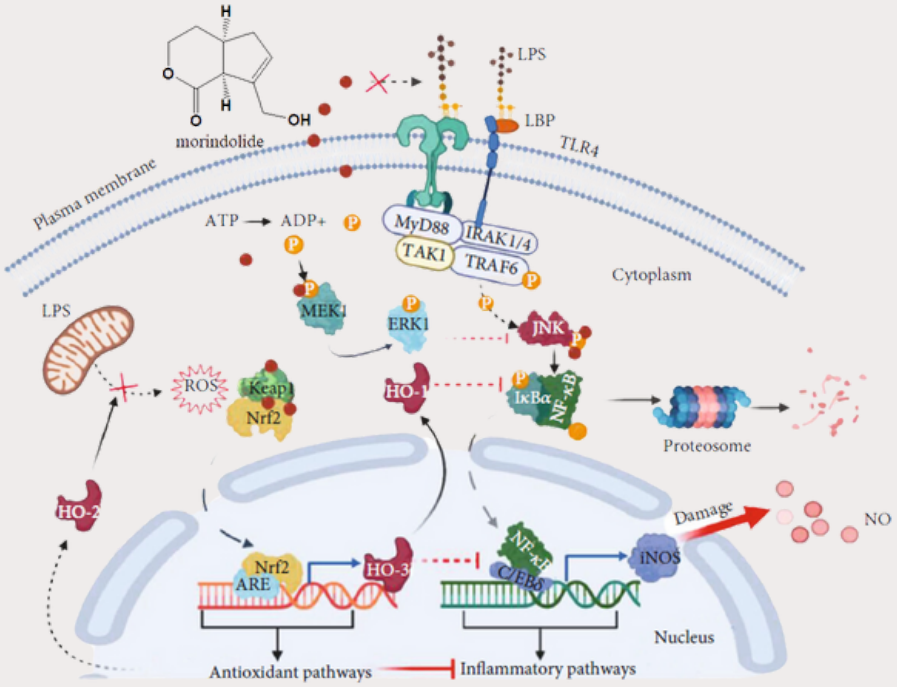
Inflammation could cause chronic, life-threatening diseases, including arthritis, diabetes, cardiovascular diseases and even cancer that are the greatest threat to human health. It is reported that non-steroidal anti-inflammatory drugs (NSAIDs) are the most common anti-inflammatory and analgesic drugs responsible for 5 to 10 % of all prescribed medications, annually. However, NSAIDs are recommended with caution, and their use should be limited to the lowest effective dose and shortest duration. In addition, common gastrointestinal, renal and cardiovascular side effects should be monitored during the use of the drugs.

Myrmecodia platytyrea

The Beers Criteria for the American Geriatric Society recommends that the chronic use of NSAIDs should be avoided because of the risk of gastrointestinal bleeding. Alternatives from natural resources especially medicinal plants are sought out due to the assumption that remedies from plants have less adverse effects.

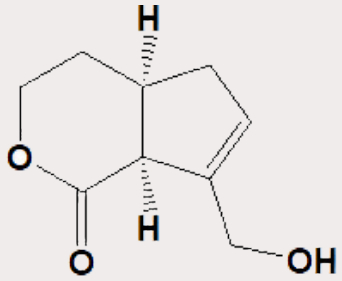
Myrmecodia platytyrea is known as Ant plant, and the tubers have been used as a decoction for managing cancer, especially in the Borneos. Thus the interest to delve into the secret ingredients of this plant has pushed our research team to investigate the therapeutic potential of *M. platytyrea* tubers for more than 10 years.

M. platytyrea has been proven to have potential due to its high antioxidant capacity and potent anti-inflammatory property.



Our studies have shown remarkable pharmacological activities of the extract. Moreover, we successfully isolated and identified an iridoid lactone named morindolide (C9H12O3) from the ethyl acetate extract of *M. platytyrea* tuber. This iridoid lactone was also isolated from *Morinda officinalis* and *Morinda citrofolia*, medicinal plants commonly used in Traditional Chinese Medicine to treat fever and inflammation. Recent pharmacological studies implied that iridoid lactones have neuroprotective, hepatoprotective, anti-inflammatory, antitumour, hypoglycemic, and hypolipidemic activities; however, the underlying molecular mechanism is not fully elucidated, mainly for morindolide.

In this project, the molecular mechanism underlying the anti-inflammatory and antioxidant effect of morindolide will be determined to unravel the role of morindolide on the regulation of redox balance that involves signalling between the Nrf2/HO-1 pathway and the inflammatory pathway and its targeted extracellular receptors. Thus, it is expected that morindolide is the phytochemical responsible for redox-balancing modulation shown by the anti-inflammatory and chemopreventive effects of *M. platytyrea* tuber extracts.



Morindolide

With this novel knowledge, we hope to pave the way to develop alternatives from herbal remedies that can improve the management of inflammation-related diseases and enhance the quality of life of the patients, globally.

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