Extended Abstract Journal of Gastrointestinal & Digestive System 2020
Vol.10 No.8

# Digestive Diseases 2020: Total Synthesis Based on the Natural Furanonaphthoquinone Scaffold and Their Biological Activity Evaluation: Chik Wai I - Hong Kong Baptist University

**Chik Wai I**

Hong Kong Baptist University, HongKong

***Abstract***

***Abstract***

Furanonaphthoquinones (FNQs) are a group of small molecules that have been found to exhibit a variety of biological activities, including antimicrobial and anticancer activities. Their natural occurrence includes plants of the Bignoniaceae family. Bioactivity-guided fractionation and isolation of Radermachera boniana Dop led to the separation and identification of napabucasin, which is a cytotoxic FNQ that can selectively target cancer stemness and metastasis. The study of napabucasin has been extensive and according to the National Cancer Institute, napabucasin is currently involved in several active clinical trials for treating cancer, including advanced and metastatic colorectal cancer. To cope with the increasing Traditional and alternative Medicine have long been used for treating cancer. Cytotoxic phyto chemicals have been isolated from a vast variety of plants and herbal medicines and they have been developed into anti-cancer lead compound sand therapeutic drugs. Naphthoquinones (NQ) are composed of a ten-carbon skeleton and appear in the forms of 1,2-naphthoquinones and 1,4-naphthoquinones.Researchhas revealed their abilities in reducing cancer stemness and metastatic potential. A class of NQ derivatives is characterized by anaphthoquinone fused with a furanring and they are known as furano-naphthoquinones (FNQ).FNQs have demonstrated a broad spectrum of bioactivities including antitumor and antimalarial effects. They often show higher efficacy when compared to NQ sin combating pathological conditions, such as avariety of cancers including leukemia, breast, colon and lung cancers. It is believed that FNQ can be further developed into new-generation chemotherapeutic agents. Radermachera boniana Dop (Figure 1) is a Vietnam-based flowering plant belonging to the Bignoniaceae family. Bioactivity-guided fractionation and isolation led to the identification of napabucasin(BBI608), which has been regarded as a potential candidate for development of therapeutic drugs that can act directly on cancer stem cells (CSCs)to overcome the problem of chemotherapy resistance. BBI608 has aroused the interests of researchers in this area and relevant studies have been extensive. According to the National Cancer Institute, napabucasin is involved in several clinical trials foranti-cancer treatment; these include advanced and metastatic colorectal cancer. To cope with the rising demand in obtaining the compound for further research, a facile and economic total synthesis route by utilizing easily Accessed reactants as starting materials for the synthesis of FNQs has been established. Moreover, structurally modified FNQ derivatives and analogs can also be chemically synthesized with reference to the accomplished synthesis pathway. Examples are indolequinonederivatives which possess nitrogen-containing hetero cycle instead of oxygen-containing hetero cyclicFNQs. The cost of obtaining BBI608would be reduced by using the efficient total synthesis route and more derivatives and analog scan be produced for structure-activity relationship (SAR) and mechanism of Total Synthesis Based on the Natural Furanonaphthoquinone Scaffold and their Biological Activity Evaluation[1] Chik Wai I, [2] Kwan Ming Lee, [3] Siu Wai Tsang, [4] HongJie Zhang[1]Hong Kong Baptist University－Institute of Research and Continuing Education, Shenzhen Virtual University Park Shenzhen, China,[2] Department of Biology, Hong Kong Baptist University, Hong Kong SAR, P.R. China, [3]Hong Kong Baptist University－Institute of Research and Continuing Education, Shenzhen Virtual University Park Shenzhen, China,[4] School of Chinese Medicine, Hong Kong Baptist University, Hong Kong SAR, P.R. China Colorectal cancer (CRC) is a disease with high incidence and mortality, constituting the fourth most common cause of death from cancer worldwide. Naphthoquinones are attractive compounds due to their biological and structural properties. In this work, 36 naphthoquinone derivatives were synthesized and their activity evaluated against HT-29 cells. Overall, high to moderate anti-proliferative activity was observed in most members of the series demand of an effective synthesis resulting in the generation of a reliable model ($r2 = 0.99$ and $q2 = 0.625$). This model allowed proposing five new compounds with two-fold higher theoretical anti-proliferative activity, which would be worthwhile to synthesize and evaluate. Further investigations will be needed to determine the mechanism involved in the effect of most active compounds which are potential candidates for new anticancer agents approach for the lead compound for its further development into a drug candidate, a facile and economic total synthesis route has been established. Moverover, derivatives of napabucasin have been synthesized in order to study the structure-activity relationship (SAR) so as to provide evidence for lead optimization and also for unraveling the mechanism of action.

This work is partly presented at 5th International Conference on Digestive system and Metabolic Diseases November on 23-24, 2020 Webinar