development pipeline. The big advantage of natural products (if they are used as herbal supplements or in foods) is that preliminary Safety studies occur naturally! However, natural products are often impure and may have a plethora of constituents with differing and sometimes synergistic potency and toxicity. Quite often, natural products display drug - drug interactions through inhibition or induction of drug clearance or transporter mechanisms. Robust scientific and statistical principles need to be applied to understand mechanism of action, dose response and time course data in efficacy studies combined with a sound understanding of species differences, in vitro: in vivo extrapolation and sex differences. Assay development of an appropriate bioanalytical marker, DMPK studies, efficacy studies, formulation, radiolabelling, safety pharmacology, toxicology studies and controlled batch-to-batch variability, are all needed to allow regulators, ethics committees and clinicians to permit clinical administration based on an adequate safety margin in animal studies. This presentation will discuss some of the issues encountered when developing natural products as novel drug candidates.

References

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O24 Functionality of selected seaweed extracts on selected pharmaceutical applications
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Cosmetic and pharmaceutical industry is looking more and more for natural marine compounds with key identified bioactivities. The Laboratoires Gilbert are a major French industrial player developing natural origin products in cosmetic and pharmacy markets. ALGAIA is a French company providing R&D services and natural extracts from macro- and micro-algae. The present study is based on a private close collaboration between the Laboratoires Gilbert and ALGAIA. The main approach has been to extract, characterise and test bioactivities of novel seaweed extracts towards cosmetic and pharmaceutical applications. In the overall work, 1 green species, 2 red species and 3 brown seaweed species have been used as starting material for creating more than 50 different extracts. After characterization, these extracts have been screened for different bioactivities, each one implemented with different techniques. In the present work, some of the outcomes related to the brown seaweed species studied will be presented and discussed. The focus will be made between the main composition of the selected extracts including polysaccharides and phenolic compounds and their anti-inflammatory and wound healing activities in particular. The composition between the three species is by nature different also the compounds extracted vary also by their yields and size, depending on the extraction process used. As a consequence, in our study, the results on each bioactivity tested show different levels and scope of action dependent upon the extract that has been tested. Those results will be presented and discussed in order to propose hypotheses of actions and constitute a strong base for sustainable development of innovative pharmaceutical products based on active seaweed extracts.

References

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O26 Screening active components of Modified Xiao Yao Powder for chemoprevention in breast cancer cells: Involvement of the NRF2/NQO1 signalling pathway
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Nuclear factor (erythroid-derived 2)-like 2 (NRF2) regulates phase II detoxifying enzymes, such as NAD(P)H: quinone oxidoreductase 1 (NQO1), by binding to the antioxidant response element (ARE). Modified Xiao Yao Powder (MXP) is most frequently used in the prevention and treatment of breast cancer in traditional Chinese medicine (TCM) prescriptions. This study aimed to investigate the role of MXP components in chemoprevention and antioxidant stress response, and the involvement of the NRF2-NQO1 signalling pathway. A total of 25 compounds contained in MXP were screened using an ARE-luciferase reporter. The most potent ARE-luciferase inducers were chosen to further examine their effects on NRF2 and
NQO1 in MCF-7 cells. These results were then confirmed by determining the oxidative stress levels. The chemopreventive effect on inhibiting carcinogenesis transformation was tested using the soft agar assay in NRF2 knockdown (NRF2KD) and wild-type MCF-10A cells. The results showed that quercetin, kaempferol and atracylenolide II were all potent NRF2 inducers, and could upregulate the expression of NRF2 and NQO1. In addition, these components could reduce oxidative stress and inhibit carcinogenesis transformation, which depended on NRF2-NQO1 pathway. In this study, we not only identified the active components of MXP but also provided mechanistic insight into the activities of these components. Our results firstly demonstrate that the NRF2-NQO1 pathway plays an essential role in mediating the activity of these compounds. Besides, atracylenolide II is a NRF2 inducer. Collectively, this study helps lay the foundation for identifying the chemoprevention properties of MXP and its active components.

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O27 Chemopreventive activities of kolaviron, a novel bioflavonoid from the seed of Garcinia kola: Mechanistic perspectives
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Compelling evidence arising from both pre-clinical and clinical investigations indicate that plant-based diets rich in a wide variety of fruits and vegetables are effective in preventing premalignant lesions. Thus the search for novel chemopreventive agents of physiological relevance acting on specific and/or multiple molecular and cellular targets hold promise as a rational strategy for the control of health threatening diseases such as cancer. Kolaviron, a natural antioxidant biflavonoid isolated from the seed of Garcinia kola (Guttiferae) indigenous to West Africa elicited striking inhibitory effects on diverse biochemical and molecular events associated with the multistage process of carcinogenesis. Specifically, kolaviron upregulated antioxidant defence capacity, modulated gene expression, signal transduction mechanisms and reduced in vivo markers of oxidative damage to lipids, proteins and DNA. Furthermore, kolaviron suppressed Dimethylnitrosamine-induced oxidative damage and expression of cyclooxygenase-2 and inducible nitric oxide synthase by inhibiting nuclear factor kappa B and activator protein-1 in rat liver. Kolaviron elicited antiproliferative properties by inhibiting the growth and survival of both colon adenoma (LT97) and carcinoma cells (HT29). Kolaviron inhibited the induction of stress-inducible proteins clusterin and heat shock proteins apoptosis-related proteins, caspase-3 and caspase-9, Fas and Fas-L induced by ethylene glycol monomethyl ether in rats testes. Kolaviron prevented Atrazine-induced changes in the expressions of p53, Bax, Bcl-2, p21, and mRNA levels of caspase-3 and caspase-9 in SH-SY5Y human neuroblastoma cell line. This novel phytochemical exerts chemopreventive effects by modulating intracellular signalling cascades and apoptotic proteins and therefore qualifies as a new therapeutic strategy for chemoprevention in chronic inflammation-related diseases.

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Session 10: Translating novel pathways – Inflammation

O28 Importance of pro-inflammatory immune lymphocyte Th17 in antitumoral properties of resveratrol, a polyphenol of wine
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Numerous epidemiological studies show that various polyphenols may protect against various diseases such as vascular diseases, cancers and inflammatory pathologies. One of the best known is the polyphenol resveratrol which is a trans-3',4',5'-trihydroxystilbene, which appears to be of great interest in the prevention of these