PLANT SUBSTANCES AS ALTERNATIVES FOR ANIMAL PRODUCTS IN TRADITIONAL MEDICINES

EXECUTIVE SUMMARY

An investigation of plant species as alternatives to the use of products obtained from endangered animal species (bear bile, rhino horn and tiger bone) was undertaken with financial support from the Department for Environment Food and Rural Affairs (Defra) and the International Fund for Animal Welfare (IFAW). The research was carried out by Middlesex University (UK) in collaboration with the Jodrell Laboratory, Royal Botanic Gardens, Kew (UK).

Products from several endangered species are used in Traditional Chinese Medicine for a variety of purposes. Bear bile (Xiong Dan) and rhino horn (Xi Jiao) are primarily classified as anti-inflammatory and fever-reducing remedies and tiger bone (Hu Gu) has been used as an anti-rheumatic/anti-arthritic remedy; the pathology of arthritis also involves inflammatory mechanisms. With the popularity of Traditional Medicine increasing, a continued demand for these products poses an ongoing and major threat to the survival of these species, all of which are listed under Appendix I of CITES. This study was undertaken in response to a recognised need for more research into possible herbal alternatives.

Based on both traditional use and scientific evidence for pharmacological actions, single herbs and TCM 'prescriptions' (combinations of herbs) were selected for investigation as alternatives to the use of bear bile, rhino horn and tiger bone in Traditional Chinese Medicine. A selection of 7 single herbs and 2 prescriptions were chosen for investigation as potential alternatives to bear bile; 9 single herbs and 6 prescriptions as potential alternatives to rhino horn; and 19 single herbs and two prescriptions as potential alternatives to tiger bone. As all three animal products are traditionally used to treat conditions associated with inflammatory processes, this area was chosen for investigation. The inflammatory response is a complex cascade of events, often triggered by infection (commonly by bacteria) and is one of the body's defence mechanisms in fighting disease. The inflammatory response forms one of the underlying pathologies of arthritis, fever; liver diseases, cancer and cardiovascular diseases. Therefore, preliminary studies were conducted to assess the effects of crude extracts, fractions and isolated compounds on bacterial growth and an anti-inflammatory mediator, nuclear factor-kappaB (NF-κB) *in vitro*. Cytochrome P450 3A4 inhibition tests were conducted to determine the effect of herbal extracts on this drug metabolising enzyme *in vitro*.

When recommending potential herbal alternatives it is essential to ensure that the correct plant species is being proposed. Verification of the plant material was carried out by comparing the chemical profiles of the samples obtained for

research from commercial sources with chemical profiles of authentic and reference material from the Chinese Medicinal plant Authentication Centre, Royal Botanical Gardens, Kew. In addition, pesticide residues and metal concentrations were determined to confirm the quality of the product.

Several of the herbs chosen for investigation as possible alternatives to bear bile were found to possess anti-bacterial activity (*Anemarhena asphodeloides Bge*, *Gardenia jasminoides* Ellis, *Scutellaria baicalensis* Georgi, *Phellodendron amurense Rupr.*, *Coptidis chinensis* Franch. and *Rheum palmatum* L). Extracts of three herbs were also shown to have anti-inflammatory properties through the inhibition NF-κB transcription of IL-6 (*Scutellaria baicalensis*, *Rheum palmatum* and *Coptis chinensis)*. Preliminary results from the cytochrome P450 3A4 inhibition studies suggest that possible herb-herb interactions may occur in preparations containing both Coptis chinensis and *Scutellaria baicalensis* (such as *Dia-Orengedokuto* and *Orengedokuto*). Also, drug-herb interactions may occur when herbal preparations containing *Coptis chinensis* and/or *Scutellaria baicalensis* are co-administered with some pharmaceutical drugs, which are metabolised by this enzyme. Further work is required to investigate the extent these effects.

Water extracts of rhino horn did not demonstrate anti-bacterial or anti-inflammatory properties, nor did they have any effect on the drug metabolising enzyme, cytochrome P450 3A4. However, certain Traditional Chinese Medicine prescriptions, both with and without rhino horn, did show anti-bacterial and anti-inflammatory properties in the assays used in this study. Further work using other bioassays is required to ascertain the contribution of the horn extracts to any activity shown by the prescriptions. The majority of herbs chosen as possible alternatives to rhino horn showed some anti-bacterial activity (17 out of 20). Extracts of several single herbs were also shown to have anti-inflammatory properties through the inhibition NF-κB transcription of IL-6 (*Paeonia suffruticosa* Andr., *Trichosanthes kirilowii* Maxim., *Lophatherum gracile* Brongn., *Acorus calamus*, *Paeonia veitchii* Lynch, *Isatis indigotica* Fort., *Glycine* max L. and *Rehmannia glutinosa* Steud*)* as well as extracts of two prescriptions (Xi jiao Dihuang Tang and Qing Ying Tang). To date, no scientific literature has been found suggesting that *Lophatherum gracile* has an anti-inflammatory effect and further studies are required to confirm these findings. *Salvia miltiorrhiza*, *Rehmannia glutinosa*, as well as *Scutellaria baicalensis* and *Coptis chinensis*, showed inhibition of cytochrome P450 3A4. Since they are commonly used TCM herbs, further work may be required to determine potential adverse interactions with other remedies or orthodox medicines.

Preliminary results suggest that tiger bone may possess some anti-inflammatory properties through the inhibition of IL-6 transcription by NF-κB. Three herbs included in existing Traditional Chinese Medicine prescriptions containing tiger bone also showed anti-inflammatory activity in the same assay *Angelica dahurica* Maxim., *Taxillus cinensis* (DC.) Danser and *Angelica sinensis* (Oliv.).. None of

the herbs investigated as alternatives to tiger bone were found to affect cytochrome P450 3A4 activity.

Supported by evidence of efficacy as anti-inflammatory and anti-bacterial agents as measured in this study, by information obtained from the available scientific literature, and by Traditional Chinese Medicine theory, a number of prescriptions and single herbs have been selected as suitable alternatives to the use of bear bile, rhino horn or tiger bone in Traditional Chinese Medicine. Most of the suggested herbal 'alternatives' to the animal products were found to already form part of one or more traditional prescriptions containing the animal products. This finding confirmed the practice in Traditional Chinese Medicine of combining remedies with similar functions for their additive and synergistic effects.

The inflammatory response is a complex cascade of events and nuclear factor-kappaB is only one anti-inflammatory mediator amongst many. Further studies are warranted to assess other pharmacological mechanisms through which the plants might mediate anti-inflammatory effects. Further work should also be carried out to investigate further the effect of herbal extracts on drug metabolising enzymes such as cytochrome P450 3A4.

If the findings of this study are to impact upon the use of products from endangered animal species in Traditional Chinese Medicine, the suggestions made for herbal alternatives will need to be acceptable to practitioners in terms of philosophy as well as potential efficacy. It will be necessary to discuss the findings of this study with TCM practitioners to determine whether the selected plant species would be considered suitable for use in Traditional Chinese Medicine as alternatives to bear bile, rhino horn and tiger bone. The suggested herbs and the evidence to support these suggestions will then need to be disseminated to practitioners and the public, both via scientific publications and through the more popular Traditional Chinese Medicine literature.