Bioactive extracts derived from fruits (*Prunus avium* and *Opuntia ficus indica*) as potential natural anti-inflammatory modulators in inflammatory bowel diseases

S. Nunes[a], A.T. Serra[a,b], M.R. Bronze[b,c], A.L. Simplício[a,b], A.A. Matias[a,b,*], C.M.M. Duarte[a,b]

[a]*Universidade Nova de Lisboa, Portugal*
[b]*Instituto de Biologia Experimental e Tecnológica, Portugal*
[c]*iMED, Faculdade de Farmácia da Universidade de Lisboa, Portugal*
E-mail address: amatias@itqb.unl.pt (A.A. Matias)

Inflammatory Bowel Disease (IBD) is characterized by a chronic inflammation derived from an uncontrolled response of the intestinal immune system against the normal enteric microflora.

There are evidences that the regular consumption of polyphenols in early life could reduce or delay IBD development in humans, by modulating the intestinal inflammation.

Sweet cherries (*Prunus avium*) and cactus pear (*Opuntia ficus indica*) are known for their high polyphenolic composition that exhibit anti-oxidant and anti-inflammatory properties. Several studies have demonstrated that cherries regular intake decrease inflammatory markers like C-reactive protein and nitric oxide (NO) and it has been reported that anthocyanins extracted from these fruits exhibit strong anti-inflammatory activity by inhibition of cyclooxygenase (COX) activities, scavenging NO radicals and decreasing TNF-α expression. Moreover, cactus pear properties are correlated with their polyphenolic composition, namely betalains.

The aim of this study was to i) develop natural crude extracts from Portuguese fruits for further fractionation using clean technologies in order to obtain *bioactive-rich concentrates* (*BRC*) and ii) evaluate their anti-inflammatory properties on *in vitro* enterocytes model stimulated with specific inflammation inducers (LPS, TNF-α and combination).

The selected fruits (*Saco* cherry variety and cactus pears) were submitted to an hydroalcoholic extraction, followed by an adsorption separation process and the fractions obtained were further characterised in terms of bioactive compounds, namely polyphenols, anthocyanins and terpenes, using colorimetric assays (Folin Ciocalteau and pH differential method) and chromatographic techniques (HPLC-DAD-UV, HPLC-DAD-ED and TLC).

The inflammatory response of the fractioned extracts was assessed using a Caco-2 single cell culture after different combinations of proinflammatory stimulus (LPS and TNF-α) regarding to release of proinflammatory markers (IL-8 and IL-1β) and monolayer integrity and permeability (basal expression of CD98 glycoprotein and determination of transepithelial electrical resistance values respectively).

Keywords: *Prunus avium*, *Opuntia ficus indica*, IBD

doi:10.1016/j.ejphar.2011.09.256

Comparing the analgesic effects of topical *Zingiber officinale* and diclofenac ointment

M. Nikbakht

Kashan University of Medical Sciences, Iran
E-mail address: drnikbakht@kaums.ac.ir

Introduction: Physical pain is one of the major sources of anxiety and inability. It is also the most common cause of leading patients to physicians. Relieve of pain is, therefore, an undeniable ultimate objective of medical sciences. For centuries, analgesics have been used to relieve pain, the most well-known causes of which are various musculoskeletal disorders. The prevalence of these musculoskeletal complaints has motivated attempts to minimize the burden of their evaluation and therapy. A few drug families such as non steroidal anti inflammatory drugs, opioid drugs, and corticosteroids have also been used to relieve musculoskeletal pains. The use of each of these results in specific complications and sometimes forces scholars to search for and introduce new drugs with fewer side effects.

Purpose: The main objective of the present study was to specify and to compare the analgesic effects of topical *Zingiber officinale* and Diclofenac ointment in the treatment of musculoskeletal pains.

Material and methods: The study was a clinical trial carried out in Kashan, central Iran, and the participants were all patients with musculoskeletal pains who were older than 15. Patients were divided in two groups. The first group received Diclofenac ointment whereas for the second group topical *Z. officinale* (mixed with water) was prescribed over the treatment period. The analgesic effects of the two drugs were studied and compared after a week of usage.

Results: The analyses of the collected data showed that the analgesic effect of Diclofenac ointment was significantly lower than that of topical Zingiberance ($p<0.0001$). The difference between male and female participants was not found to be statistically significant in any of the treatment groups.

Conclusion: *Zingiber officinale* appears to be as Diclofenac ointment in the treatment of musculoskeletal pains and may offer safer alternative to the use of topical Diclofenac.

Keywords: Physical pain, Zingiberanc, Diclofenac

doi:10.1016/j.ejphar.2011.09.257

Lipopolysaccharide induces anhedonia-like reward deficits, reflected by long-term increases in brain stimulation reward thresholds

J. Prins*, F. van Heesch, L. de Haan, B. Olivier, A.D. Kraneveld, S.M. Korte

Utrecht University, Netherlands
E-mail address: j.prins1@uu.nl (J. Prins)

Anhedonia is one of the core symptoms of major depressive disorder (MDD) and is characterized by the inability to experience pleasure. The role of inflammatory processes in MDD, and more specifically anhedonia, has been extensively reviewed. The endotoxin lipopolysaccharide (LPS) induces sickness behaviour 6 h after injection, while depressive-like behaviour as measured by a decreased preference for sucrose is expressed 24 h after administration. To better investigate the time-course in which anhedonia symptoms emerge, the sucrose preference test might not be of best choice, because of the possible interfering appetite-suppressing effects of LPS, at least at time points at which sickness behaviour is still apparent. Therefore, the aim of the current study was to determine the onset of reward-related disturbances of LPS on intracranial self stimulation (ICSS) thresholds. Bipolar stimulating electrodes were implanted into the lateral hypothalamus of male Wistar rats, and animals were trained in a discrete-trial current-threshold ICSS procedure. After stable ICSS thresholds were established, eight animals were treated with LPS (250 μg/kg, i.p.); nine animals were treated with vehicle (0.9% NaCl) as control. Animals were tested in the ICSS paradigm 1 h, 4 h, 24 h and up to 14 days after administration. Our study showed significant elevations of ICSS thresholds up to 72 h after LPS administration, reflecting a decreased activity of brain reward circuitry and desensitization of the rewarding effects of ICSS and suggest an anhedonic state of the animal. The present study showed, to our knowledge for the first time, that LPS induces an anhedonic state up to 72 h after injection with a maximum at time point 4 h. The fact that response latencies were not affected suggested that the used dose of LPS did not induce motor deficits in the animals. More work is clearly needed