Evaluation on Antioxidant, Anti-inflammatory and Neuroprotective Activities and Chemical Contents of Species used Traditionally for Inflammation in Turkey

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in mice with CD induced by 1-fluoro-2,4- dinitrobenzene (DNFB). Moreover, the anti-inflammatory effects on production levels of prostaglandin E2 (PGE2) and nitric oxide (NO), and expression levels of cyclooxygenase 2 (COX-2) and inducible nitric oxide synthase (iNOS) were investigated in RAW 264.7 cells. Topical application of ALE effectively prevented ear swelling induced by repeated DNFB application. ALE prevented epidermal hyperplasia and infiltration of immune cells and lowered the production of interferon (IFN)-gamma, tumour necrosis factor (TNF)-alpha and interleukin(IL)-6 in inflamed tissues. In addition, ALE inhibited expression of COX-2 and iNOS and production of NO and PGE2 in RAW 264.7 cells. These results indicate that *Artemisia* leaf can be used as a therapeutic agent for inflammatory skin diseases, and that its anti-inflammatory effects are closely related to the inhibition of inflammatory mediator release from macrophages and inflammatory cytokine production in inflamed tissues.

P-268 Probing the anti-inflammatory activity of tormentil rhizome (*Potentilla erecta* (L.) Raeusch., rhizoma)

Authors Maria Pigott[1], Ismael Obaidi[1], Elaine Dempsey[2], Cillian Jacques Gately[1], Michael Carty[3], Sinéad C. Corr[2], Helen Sheridan[1]
Institutes **1** NatPro Centre, School of Pharmacy and Pharmaceutical Sciences, Trinity College Dublin, Dublin, Ireland; **2** Dept. of Microbiology, School of Genetics and Microbiology, Trinity College Dublin, Dublin, Ireland; **3** School of Biochemistry and Immunology, Trinity Biomedical Sciences Institute, Trinity College Dublin, Dublin, Ireland
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Traditional herbal medicinal products of *Potentilla erecta* (L.) Raeusch., rhizoma (tormentil rhizome) are indicated for symptomatic treatment of mild diarrhoea or minor inflammations of the oral mucosa exclusively based upon long-standing use. Tormentil's utility is largely attributed to the astringent effects of the rhizome's high tannin content but there are also non-clinical reports of the antimicrobial, antioxidant, anti-inflammatory and immunostimulatory effects of tormentil that may contribute to its pharmacology. In this study, we probed the anti-inflammatory effects of tormentil rhizome in vitro and in a dextran sodium sulfate (DSS) mouse model of colitis. A methanolic extract was screened for effects on lipopolysaccharide induced cytokine release in human THP-1 cells and in murine immortalised bone marrow derived macrophages (iBMDMs). In phorbol 12-myristate 13-acetate differentiated THP-1 cells, tormentil reduced the production of TNF-α, IL-1β, IL-6 and RANTES on stimulation. Somewhat contradictory results were found in murine iBMDMs, whereby treatment caused a dose dependent increase in TNF-α with no significant change in IL-6 or RANTES. In line with this, tormentil treatment in the DSS model increased TNF-α in the proximal colon tissue of the DSS group and also increased IL-1β and IL-10 significantly. Despite these changes, a small but significant reduction in colitis severity, as demonstrated by the reduced Disease Activity Index, was observed on the last day of the experiment. Furthermore, tormentil treatment increased basal IL-10 in the proximal colon of healthy control animals. Taken together, these results support further work to unravel the mechanism underlying the immunomodulatory effects of tormentil rhizome extract.

P-269 A combination of *Zingiber officinale* root extract and cannabidiol exhibits potent anti-inflammatory effects and ameliorates clinical symptoms of atopic dermatitis

Authors Martin Kragl[1], Christine Neubauer[1], Kathrin Moritz[1], Ramona Ziegler[1], Nicole Mähler[1], Michael Soeberdt[1], Ehsan Bonyadirad[2], Theodor Braun[3], Przemyslaw Filipek[3], Thomas Jakschitz[3], Andreas Koeberle[2], Günther Bonn[3], Christoph Abels[1]
Institutes **1** Bionorica SE, Neumarkt, Germany; **2** Michael Popp Institute, Innsbruck, Austria; **3** Austrian Drug Screening Institute (ADSI), Innsbruck, Austria
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Potential anti-inflammatory and anti-oxidative activities of 24 plant extracts displaying different polarities were screened in various in vitro assays and applied to a principal component analysis. Cannabidiol (CBD) and a *Zingiber officinale* root (ginger) extract were found to be extraordinarily active.
In subsequent studies on TNF-α-stimulated NF-κB activation [1], poly(I:C)-stimulated cytokine and chemokine secretion from human epithelial primary cells and cell lines, their anti-inflammatory activities were confirmed. Notably, the combination of CBD and ginger consistently enhanced the anti-inflammatory effects, accompanied by an increased release of the endocannabinoid anandamide. A positive modulation of the endocannabinoid system is relevant for effects regarding inflammation and pruritus [2, 3]. Subsequently, an O/W emulsion containing CBD and ginger was developed and investigated in a clinical trial including 44 subjects with history of atopic eczema and itching score of at least 1. Efficacy and tolerability were evaluated at baseline and after 5 days of product application. A statistically significant reduction of erythema, skin dryness and trans epidermal water loss was observed, whereas skin moisture increased significantly. Subjective evaluation of an itch using a numeric rating scale [4] showed a continuous decrease that was significantly reduced from day 2 onwards. The product was very well tolerated.
In summary, identification of CBD and *Zingiber officinale* root extracts with proven antioxidative and anti- inflammatory activities enabled the development of a new O/W emulsion which improved key symptoms of dry and eczema-prone skin clinically.
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Conflict of Interest This study was supported by industrial research grants, and several of the authors (CA, CN, KM, MK, MS, NM, and RZ) are employees of the sponsor. CA and MS are named as inventors on a patent application for compositions containing cannabidiol and an extract from ginger.
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P-270 Evaluation of antioxidant, anti-inflammatory and neuroprotective activities and chemical contents of species used traditionally for inflammation in Turkey

Authors Burcu Sen[1], Sukran-Kubra Ilhan[1, 2], Buge Erel[3, 4], Zulfiye Gul[3], Timucin Avsar[5], Hilal Bardakci[6, 7], Alexandra K. Kiemer[8], Britta Diesel[8]
Institutes **1** Istanbul University, Faculty of Pharmacy, Department of Pharmacognosy, 34116, Istanbul, Turkey; **2** Logo Pharmacy, 34510, Istanbul, Turkey; **3** Bahcesehir University, Faculty of Medicine, Department of Medical Pharmacology, 34734, Istanbul, Turkey; **4** Novartis Turkey, Business Excellence & Execution – Customer Strategy (CX) & Digital, 34805, Istanbul, Turkey; **5** Bahcesehir University, Faculty of Medicine, Department of Medical Biology, 34734, Istanbul, Turkey; **6** Acibadem Mehmet Ali

Aydınlar University, Faculty of Pharmacy, Department of Pharmacognosy, 34684, Istanbul, Turkey; 7 Fenerbahce University, Faculty of Pharmacy, Department of Pharmacognosy, 34758, Istanbul, Turkey (current address); 8 Saarland University, Department of Pharmacy, Pharmaceutical Biology, 66123, Saarbrücken, Germany
DOI 10.1055/s-0043-1774141

The pathophysiology of Parkinson's disease (PD) is linked to accumulation of the cytoplasmic structures called Lewy bodies with their main constituent being α-synuclein oligomers. Recent studies showed that α- synuclein overexpression is associated with microglial activation, neuroinflammation, and neurodegeneration. In order to protect neurons and prevent disease progression, studies on agents that are effective on α-synuclein expression, whose oligomers cause cell damage by initiating neuroinflammation, and therefore anti-inflammatory and antioxidant agents, are increasingly important [1].

This study aimed to determine antioxidant, anti-inflammatory, and neuroprotective activities of various extracts of *Clematis vitalba*, *Ecballium elaterium* (EE), *Fraxinus ornus* subsp. *ornus* (FOO), *Paliurus spina- christi* and *Sambucus ebulus* (SE), which might indicate a therapeutic potential for treatment of inflammatory disorders like PD. FOO showed the highest antioxidant activity by DPPH method. FOO, SE and EE extracts exhibited higher anti-inflammatory potential since they reduced nitric oxide and TNF-production by Griess assay (using LPS-activated RAW 264.7 macrophages) and TNF bioassay (using L929 cells), and were found to be rich in flavonoid and phenolic compounds chromatographically. Therefore, their protective activities on the toxicity induced by rotenone and A-53T-α-synuclein plasmid were tested by analysis of the change in α-synuclein expression, its effect on the cell lines and cell viability analysis through xCELLigence. Only FOO cortex extract was protective and decreased the cell death. Our findings indicate that FOO has good anti-inflammatory and neuroprotective activity. Further studies are required to assess its potential applications in the treatment of inflammatory disorders like PD.

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P-271 Chalcones from *Melodorum fruticosum* inhibit microsomal prostaglandin E2 synthase-1 (mPGES-1) and 5-lipoxygenase (5-LO)

Authors Birgit Waltenberger[1], S. Engels[1, 2], Veronika Temml[3], Loi Huynh[4, 5], Hung Tran[4], Oliver Werz[6], Andreas Koeberle[7]

Institutes 1 Institute of Pharmacy/Pharmacognosy and Center for Molecular Biosciences Innsbruck (CMBI), University of Innsbruck, Innsbruck, Austria; 2 Department of Extract(ion) Research and Phytoanalytics, Bionorica research GmbH, Innsbruck, Austria; 3 Department of Pharmaceutical and Medicinal Chemistry, Paracelsus Medical University Salzburg, Salzburg, Austria; 4 Department of Pharmacognosy, Faculty of Pharmacy, University of Medicine and Pharmacy, Hô` Chí Minh, Vietnam; 5 School of Medicine and Pharmacy, University of Danang, Da Nang, Vietnam; 6 Chair of Pharmaceutical/Medicinal Chemistry, Institute of Pharmacy, Friedrich-Schiller-University, Jena, Germany; 7 Michael Popp Institute and Center for Molecular Biosciences Innsbruck (CMBI), University of Innsbruck, Innsbruck, Austria
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Melodorum fruticosum (Annonaceae) is used in traditional Vietnamese medicine to aid digestion and has previously been shown to inhibit interleukin-8 (IL-8) release in human neutrophils [1]. Herein, we report additional anti-inflammatory features of this medicinal plant. At 30 µg/mL, the dichloromethane (DCM) extract of *M. fruticosum* leaves inhibited microsomal prostaglandin E_2 synthase-1 (mPGES-1), which catalyses the formation of prostaglandin E_2, to 11.5 % residual activity. Moreover, at the same concentration, it also inhibited 5-lipoxygenase (5-LO), an enzyme catalysing the formation of leukotrienes (LT), to a residual activity of 19.4 %. To identify the constituents which might be responsible for these anti- inflammatory activities, fifteen constituents isolated from the bioactive DCM extract *of M. fruticosum* were analysed for their inhibitory activities on mPGES-1 and 5-LO. The benzylated chalcone 2′,4′-dihydroxy-4,6′-dimethoxy-3′(2″-hydroxybenzyl)chalcone and its corresponding dihydrochalcone, also known as MF-15, were most active against mPGES-1 with IC_{50} values of 2.6 and 1.8 µM, respectively. The benzylated dihydrochalcone MF-15 showed also the highest activity against 5-LO (IC_{50} = 3.4 µM), together with 2′,4′- dihydroxy-4,6′-dimethoxychalcone, 2',4'-dihydroxy-4,6'-dimethoxydihydrochalcone, and 2′,6′-dihydroxy-4′- methoxychalcone, inhibiting 5-LO with IC_{50} values between 9.6 and 12.2 µM. The obtained inhibitory activities against mPGES-1 and 5-LO were supported by docking studies which revealed putative binding modes of the bioactive natural products in the active sites of the enzymes. The findings of this study show that *M. fruticosum* possesses promising anti-inflammatory activity via multiple pathways and points of attack.

Conflict of Interest The authors declare no conflict of interest.

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P-272 Effects of Iso-mukaadial acetate on glucose homeostasis, insulin secretion and haematological function in streptozotocin-induced diabetic rats

Authors Nontokozo Msomi[1], Murtala Isah[2], Mohammed Ibrahim[3], Mthokozisi Simelane[4]

Institutes 1 University of KwaZulu Natal, Durban, South Africa; 2 Umaru Musa Yar'adua University, Katsina, Nigeria; 3 Ahmadu Bello University, Zaria, Nigeria; 4 University of Johannesburg, Johannesburg, South Africa
DOI 10.1055/s-0043-1774143

Diabetes is a chronic, progressive metabolic disorder which is becoming a global health risk, as its prevalence is increasing steadily worldwide. *Warburgia salutaris* (Bertol. f.) Chiov. [Canellaceae] is traditionally used to treat diabetes. The use of hypoglycaemic plants to manage this condition is a common practice in developing countries. In the present study, iso-mukaadial acetate (MA) from the ground stem bark of *W. salutaris* was evaluated for its effect on blood glucose, insulin level and haematological parameters in a streptozotocin (STZ) induced diabetic rat model. Male Sprague-Dawley rats were randomly divided into untreated and treated groups with MA (0.5, 1.5 and 2.5 mg/kg), acarbose (10 mg/kg) and crude extract (1.5 mg/kg). Diabetes was induced in the diabetic group and treatment was administered for five days (Days 8-12). Treatment with MA improved body weight, white blood cells, haemoglobin and eosinophil levels with a moderate decrease in neutrophils in comparison to the diabetic control animals. MA at its lowest dose (0.5 mg/kg) improved red blood cell production and significantly increased lymphocytes, with a marginal decrease in monocytes in comparison to the diabetic control animals. It was further observed that MA at its lowest dose decreased blood glucose concentration and slightly increased insulin level, compared to the highest doses of MA. The data of this study suggests that administration of iso-mukaadial acetate at its lowest concentration modulates diabetes-induced haematological changes. However, further experimental studies are required to substantiate its relevant therapeutic effects.

P-273 Anti-obesity effects of *Philadelphus tenuifolius* extract via improvement of lipid metabolism in high-fat diet-induced obese mice

Authors Yoon-Young Sung[1], Mi-Sun Kim[1], Heung Joo Yuk[1], Seung-Hyung Kim[2], Geung-Joo Lee[3], Dong-Seon Kim[1]

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