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Insights into research on the anti-inflammatory and antinociceptive activities of *Scandix iberica Bieb.*

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It is thought that bioactive compounds from plant foods may have beneficial health effects and decrease the risk of chronic inflammatory diseases. In Turkish folk medicine, flowers of the *Scandix iberica* Bieb. (*Apiaceae*) have been used to combat rheumatic pain. The aim of this study is to appraise the anti-inflammatory and antinociceptive activities of the different types of extracts prepared from S. iberica carrageenan, Prostaglandin E2 (PGE2) and serotonin-induced hind-paw oedema, acetic acid-induced capillary permeability and 12-O-tetradecanoyl-phorbol-13-acetate (TPA)-induced mouse-ear oedema models were used to appraise anti-inflammatory activity. Antinociceptive activity was tested using a p-benzoquinone induced abdominal constriction method. Among the extracts, only the n-Hexane extract was shown to possess a noticeable anti-inflammatory and antinociceptive activity in mice without inducing any gastric damage at 100 and 200 mg/kg doses, while the rest of the extracts were entirely inactive. The activity of the n-Hexane extract led to a greater appreciation of some phenylpropanoids, mainly estragole (88.90%), through Capillary Gas Chromatography-Mass Spectrometry (GC-MS).

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Design and synthesis of new 2-substituted benzimidazoles as dual inhibitor for c-Met and VEGFR-2

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C-Met (a receptor tyrosine kinase) has been shown to collaborate synergistically with VEGFR-2 (a member of vascular endothelial growth factor receptors belonging also to tyrosine kinase), resulting in promoting development of angiogenesis and progression of various human cancers. In recent years, some c-Met/VEGFR-2 dual inhibitors have been reported or have entered clinical trials. For example Treanda (bendamustine hydrochloride) comprises a benzimidazole ring with a butyric acid substituent and was approved by FDA for the treatment of chronic lymphotic leukemia. The rational design of target molecules was based on its *in silico* molecular docking study and *in silico* ADMET study to provide an insight about the binding mode into binding sites of both c-Met/VEGFR-2 as a dual inhibitor. Thus, the benzimidazole ring of bendamustine was retained, buturic acid was replaced by nitro group and the bis-(chloroethyl) amine group (mechlorethamine) was substituted with several biologically active scaffolds such as oxadiazole, thiadiazole, and triazolo-thiadiazines. Five series (5a-b, 7a–o, 10a-d, 13a–b and 15a–c) of 2- substituted benzimidazole derivatives were synthesized via condensation of 4-nitro-o-phenylenediamine with α-ketoglutaric acid. The cytotoxic activities of some of the designed analogues were carried out at the National Cancer Institute (NCI), USA; at a single dose (10 μM), against full NCI 60 human cell lines. Most of the tested compounds, 5b (793196/1), 7i (793197/1), 13a (793191/1), 13f (793193/1), 13i (793192/1), 15a (793199/1) and 15b (793200/1) exhibited significant anti-proliferative activity. Further, all of the prepared compounds are under enzymatic screening for their inhibitory activity for both c-Met and VEGFR-2 as dual inhibitor.

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