

ABSTRACT

There is a high prevalence of usage of herbal medicine to treat common chronic widespread diseases. However, the scientific literature supporting the efficacy of herbal therapies is incomplete. There are few well-controlled studies that support the efficacy of herbal remedies in the treatment and clinical improvement of patients with asthma, arthritis and Alzheimer's disease. Available scientific evidence has not yet confirmed the validity of their popular role in the treatment of these diseases. The plant *Euphorbia tirucalli* Linn has been successfully used as a tribal folk medicine in India and Africa for the management of acute inflammatory, arthritic, nociceptive pain and asthmatic symptoms. Our various test extracts, plant fractions were prepared and the respective phytochemical characterisations were done. Study was conducted to assess the anti-inflammatory, analgesic, anti-asthmatic and anti-arthritic role of the total steroid and terpenoid rich fractions of the hydro-alcoholic extract of *E. tirucalli* root (STF-HAETR). STF-HAETR fraction demonstrated 71.25 ± 2.5 and $74.25 \pm 5.1\%$ protection against acetic acid-induced pain and central neuropathic pain at 75 and 100 mg/kg doses, respectively. It showed 96.97% protection against acute inflammation at 100 mg/kg with 1.6-fold better activity than the standard drug. The fraction exhibited such efficacy via inhibition of proinflammatory cytokines TNF- α , IFN- γ , by 61.12 and 65.18%, respectively, at 100 μ g/mL. Inhibition of cyclooxygenase and Nitric oxide synthase in a dose-dependent manner affirms its analgesic and anti-inflammatory activity. The spectrophotometric analysis reveals that STFHAETR induces ameliorative effect against heat-induced denaturation of Bovine serum albumin (BSA) and exhibits significant anti-proteinase activity. The plant fraction also demonstrated anti-asthmatic activity by displaying 62.45% protection against histamine induced bronchoconstriction or dyspnoea. Our findings suggest that STF-HAETR could be an effective safe therapeutic agent to treat nociceptive pain, acute inflammation, asthma, and arthritis which may authenticate its traditional use. Study was also conducted to evaluate the potential of bioactive extracts of *Trigonella foenum-graecum*, *Piper betel*, and *Lagenaria siceraria* homogenate was tested against arthritis and related inflammation. Fenugreek and betel leaf extracts showed promising anti-inflammatory and anti-arthritic potential in this research work. The anti-arthritis mechanism of extract was thought to be due to the significant inhibition and reduction of TNF- α and IL-6. At

200 µg/ml, extracts from fenugreek and betel leaf lowered the levels TNF- α and IL-6. TNF- α, the most powerful pro-inflammatory cytokine, was suppressed by fenugreek and betel leaf extract, respectively, at 200 µg /ml, by 49% (P< 0.0001) and 37% (P< 0.001). Moreover, at graded dosages, fenugreek and betel leaf showed excellent protection against a heat-induced protein denaturation cascade. In terms of protein denaturation inhibitory action, fenugreek and betel leaf had substantial IC50 values of 90 and 95 µg/ml. The inhibitory effects of Fenugreek and Betel leaf on protein denaturation were 1.34 and 1.26 times more efficient than the conventional positive inhibitor, diclofenac sodium. Betel leaf and fenugreek extract stabilized hypotonic saline caused human RBC membrane lysis by 97% and 83% at 200 µg/ml, respectively, with IC50 of 105 and 128 µg/ml, whereas bottle gourd provides 75% protection at an equal dose. With IC50 values of 20 and 23 µg/ml, respectively, betel leaf extract and bottle gourd homogenate inhibited 15-LOX enzyme activity in a dose-dependent manner. The inhibitory effects of the bottle-gourd homogenate and betel leaf extract are almost identical to those of the conventional 15-LOX inhibitor azelastine (IC50 15 µg /ml). At 100 µg /ml, bottle gourd and betel leaf extracts inhibited 15-LOX by 98 and 96 % respectively, whereas Azalastine, a conventional medication, inhibited 15-LOX by 99.5%. An in-vitro bio-assay revealed that bottle-gourd extract reduced histamine-induced bronchoconstriction. This study found that bottle-gourd extract reduced contractions elicited by histamine at 50 µg/ml in 0.4 ml tissue bath by 20%, 48.7%, and 65 percent in a dose-dependent manner at 100, 200, and 300 µg/ml concentrations, respectively. At 200 mg/kg, fenugreek and betel leaf fractions effectively protected against CFA-induced arthritic paw edema by 52% and 51% respectively, on day 28. Furthermore, in CFA induce arthritis model, at 200 mg/kg, Fenugreek and betel leaf water extract reduced arthritis index by 86 and 83%, respectively, on the 28th day, which was equivalent to the result (88% decrease of arthritis index) produced by the conventional medicine dexamethasone (0.75 mg/kg). *Gelsemium sempervirens* (L.) J.St.-Hil is a herb used for the treatment of various neuroses in both homeopathic and Ayurvedic systems. We examined whether *Gelsemium* reconstituted tincture can protect against scopolamine induced cognitive discrepancies in amnesic mouse model. In order to investigate the protective mechanism of *Gelsemium* against dementia, in vitro acetyl cholinesterase and β-secretase enzyme inhibition and estimation of glutathione level in mouse brain were carried out. The inhibition study on acetyl cholinesterase and β-secretase enzyme was

conducted on brain homogenate supernatant spectrophotometrically using specific substrate. Cognitive enhancement activity was assessed by elevated plus maze and passive avoidance study in scopolamine induced dementia mouse model. Glutathione, an anti-oxidant, was measured spectrophotometrically from scopolamine induced amnesic mice brain supernatant using 5,50-dithiobis 2-nitrobenzoic acid in the presence and absence of Gelsemium tincture. Significant inhibition was found with Gelsemium on AChE and β -secretase enzyme with an IC₅₀ of 9.25 and 16.25 mg/ml, respectively, followed by increasing glutathione levels in comparison to the untreated dementia group. The effect of Gelsemium of scopolamine-induced cognitive deficits was determined by measuring the behavioral parameters and the antioxidant status of the brain after scopolamine (1 mg/kg i.p.) injected amnesic mice. Gelsemium significantly demonstrated *in vivo* antidementia activity (60% protection) and increased exploratory behavior. Our investigations indicated that alkaloid, iridoids and coumarin enriched reconstituted Gelsemium tincture extract displays promising cognitive enhancement in adult mice after short-term oral treatment. Hence, Gelsemium can be a promising anti-dementia agent, mediating the protection against amnesia, attention disorders and learning dysfunctions through dual inhibition of both acetyl cholinesterases (no false positive effect was shown), β -secretase and antioxidant activity. This study's findings suggest that a low dose of reconstituted mother tincture of Gelsemium sempervirens may offer an emerging therapeutic option for the prevention of dementia and related neurodegenerative disorders by improving learning, and memory deficits, and brain oxidative damage in scopolamine-induced amnesic mice. According to the findings in arthritis, the bioactive fraction of STF-HAETR decreased pain by selective COX-2 inhibition and attenuated all types of inflammatory syndromes by downregulating inflammatory NO production by lowering iNOS expression, TNF-alpha, IL-6, and IL-12 cytokine levels. The anti-inflammatory and anti-nociceptive activities of carrageenan were confirmed in an *in-vivo* model of carrageenan-induced acute inflammatory paw edema, as well as acetic acid-induced peripheral and hot plate-induced central nociceptive pain model. As a result, the powerful anti-inflammatory properties of total steroid-terpenoid enriched fractions of Euphorbia tirucalli might be investigated as a viable therapeutic candidate in many inflammatory and immunological dysregulation and disorders such as asthma, arthritis, and nociceptive pain via immune modulation. The ability of test extracts of betel leaf, fenugreek and bottle gourd to lower TNF-alpha and IL-6 levels, and the

intensities of COX-2 and 15-LOX enzymes, is thought to be responsible for their anti-arthritic and anti-inflammatory properties and managing the pain. Furthermore, the asthmatic condition is reduced by bottle gourd homogenate and betel leaf aqueous extract. Because of its promising anti-oxidant efficiency, betel leaf extract exhibited anti-arthritic and anti-asthmatic potential. As a result, as validated by previous research, these bioactive extracts may be emphasized as a promising anti-inflammatory herbal medicine shortly for the therapy of diverse auto-immune disorders such as rheumatoid arthritis and allergic asthma. In this proposal an attempt was done to find out novel medicinal plants having anti-arthritic, antiasthmatic, anti-inflammatory and anti-Alzheimer potential involvement of their chemical constituents and pharmacological profile. Respective plant fractions were assessed through various in vitro and in vivo animal models of arthritis, asthma and dementia for evaluating the therapeutic prospect.