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The *Journal of Ethnopharmacology* is dedicated to the exchange of information and understandings about people's use of plants, fungi, animals, microorganisms and minerals and their biological and pharmacological effects based on the principles established through international conventions. Early people confronted with illness and disease, discovered a wealth of useful therapeutic agents in the plant and animal kingdoms. The empirical knowledge of these medicinal substances and their toxic potential was passed on by oral tradition and sometimes recorded in herbals and other texts on *materia medica*. Many valuable drugs of today (e.g., atropine, ephedrine, tubocurarine, digoxin, reserpine) came into use through the study of indigenous remedies. Chemists continue to use plant-derived drugs (e.g., morphine, taxol, physostigmine, quinidine, emetine) as prototypes in their attempts to develop more effective and less toxic medicinals.

In recent years the preservation of local knowledge, the promotion of indigenous medical systems in primary health care, and the conservation of biodiversity have become even more of a concern to all scientists working at the interface of social and natural sciences but especially to ethnopharmacologists. Recognizing the sovereign rights of States over their natural resources, ethnopharmacologists are particularly concerned with local people's rights to further use and develop their autochthonous resources.

Accordingly, today's ethnopharmacological research embraces the multidisciplinary effort in the:

- documentation of indigenous medical knowledge,
- scientific study of indigenous medicines in order to contribute in the long-run to improved health care in the regions of study, as well as
- search for pharmacologically unique principles from existing indigenous remedies.

The *Journal of Ethnopharmacology* publishes original articles concerned with the observation and experimental investigation of the biological activities of plant and animal substances used in the traditional medicine of past and present cultures. The journal will particularly welcome interdisciplinary papers with an ethnopharmacological, an ethnobotanical or an ethnochemical approach to the study of indigenous drugs. Reports of anthropological and ethnobotanical field studies fall within the journal's scope. Studies involving pharmacological and toxicological mechanisms of action are especially welcome. Clinical studies on efficacy will be considered if contributing to the understanding of specific ethnopharmacological problems. The journal welcomes review articles in the above mentioned fields especially those highlighting the multi-disciplinary nature of ethnopharmacology. Commentaries are by invitation only.

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Ginger extract and its compound, 6-shogaol, attenuates painful diabetic neuropathy in mice via reducing TRPV1 and NMDAR2B expressions in the spinal cord

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ABSTRACT

Ethnopharmacological relevance: In silico data revealed that the active compound of ginger (*Zingiber officinale* Roscoe), 6-shogaol, has strong affinity toward transient receptor potential vanilloid-1 (TRPV-1). TRPV-1 is expressed in nervous tissue and pancreatic β-cells. Prolonged induction of TRPV-1 is related to the expression of N-methyl-D-aspartate receptor subunit 2B (NMDAR2B). However, there are no data on TRPV-1 and NMDAR2B expressions in nervous tissue after 6-shogaol or ginger extract treatment nor pancreatic islet morphology and insulin expression in mice model of painful diabetic neuropathy (PDN).

Aim of the study: This study aimed to investigate the mechanism of action of ginger extract and its compound, 6-shogaol, on pancreatic islets as well as on expressions of TRPV-1 and NMDAR2B in the spinal cord of streptozotocin (STZ)-induced mice model of PDN.

Materials and methods: Sixty-four 5–6 weeks old male-Balb/C mice were induced with 110 mg/kgBW STZ i.p., while eight mice were used as control group. Mice with blood glucose level ≥200 mg/d, that suffered hyperalgesia and allodynia were classified as PDN mice. Hot plate and von Frey filament tests were performed once a week until termination. At day 28 after considered as PDN, ginger extracts, 6-shogaol or gabapentin as control treatment were given once daily for 21 days until day 49, except for the diabetic control group. Upon termination, mice' pancreas were fixed, processed as paraffin sections and stained with hematoxylin eosin. Total volume of pancreatic islets was estimated using Cavalieri methods. Immunohistochemistry on pancreatic sections were performed to observe insulin expression. mRNA was extracted from lumbar segments of the spinal cord, followed by cDNA preparation and quantitative Real-Time Polymerase Chain Reaction (qRT-PCR) to measure the expressions of TRPV1 and NMDAR2B. The mean differences between groups were analyzed using one-way analysis of variance (ANOVA) with $p < 0.05$ considered statistically significant.

Results: Ginger extracts and 6-shogaol alleviated hyperalgesia and allodynia. The groups that received ginger extract 400 mg/kgBW or 6-shogaol 15 mg/kgBW had significantly lower TRPV1 and NMDAR2B expressions in the spinal cord compared to the diabetic control group ($p < 0.001$; $p < 0.05$). However, no differences in volume of pancreatic islets ($p > 0.05$) nor insulin expression were observed in all PDN groups.

Conclusion: Ginger extracts and its compound, 6-shogaol, reduced pain symptoms in PDN via its effect on decreasing TRPV1 and NMDAR2B expressions in the spinal cord, with very limited effect on pancreatic islets.

1. Introduction

Painful Diabetic Neuropathy (PDN) is a common complication of chronic diabetes mellitus because sustained hyperglycemia causes biochemical imbalances and nerve degeneration (Singh et al., 2014). In the mice model of PDN, nociceptive receptor transient receptor potential vanilloid-1 (TRPV1) is highly expressed in peripheral nerves (C and A_δ), dorsal root ganglia (DRG) and dorsal horn of the spinal cord (Pabbidi et al., 2007, 2008). Therefore, TRPV1 becomes one of the potential targets in drug development for PDN (Brito et al., 2014). TRPV1 functionally interacts with N-methyl-D-aspartate receptors (NMDAR) and contributes to the development of pain behavior (Lee

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