JOURNAL OF HERBAL MEDICINE 4 (2014) 37–47

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/hermed

Original Research Article

Efficacy and safety of the topical use of intranasal cinnamon bark extract in seasonal allergic rhinitis patients: A double-blind placebo-controlled pilot study

Sanjiv Walanj[a], *Aparna Walanj*[a], *Vishwaraman Mohan*[b], *Prasad Arvind Thakurdesai*[b,*]

[a] *Ethika Clinical Research Centre, Prakruti Hospital, Siddheswar Arcade, Kalwa West, Thane 400605, Maharashtra, India*

[b] *Department of Scientific Affairs, Indus Biotech Private Limited, 1, Rahul Residency, Off Salunke Vihar Road, Kondhwa, Pune 411 048, India*

ARTICLE INFO

Article history:
Received 5 August 2013
Received in revised form
10 December 2013
Accepted 30 December 2013
Available online 15 January 2014

Keywords:
Type-A proanthocynidins
Cinnamon bark
Seasonal allergic rhinitis
RQLQ
Total nasal symptom scores
Work productivity

ABSTRACT

The present study was aimed at the evaluation of the efficacy and safety of an intranasal spray of a type-A proanthocynidine polyphenol based standardized hydroalcoholic extract of *Cinnamonum zylanicum* bark (TAPP-CZ) in seasonal allergic rhinitis (AR) patients using a double-blind placebo-controlled parallel design. TAPP-CZ (nasal spray, 100 μg/100 μL in each nostril, twice a day) with matching placebo were administered for 4-weeks to 40 randomized patients (20 each in TAPP-CZ and placebo groups) who suffered from severe AR. The efficacy outcome measure scores were obtained from Juniper rhinoconjunctivitis quality of life questionnaire (RQLQ) instrument, nasal symptom scores (NSS), total NSS (TNSS), Work Productivity and Activities Impairment–Allergy Specific (WPAI–AS) instrument at baseline, end of 4-week treatment, and after 4-weeks of follow-up period. The safety outcome measures included pulmonary function tests (spirometry), vital signs, hematology, biochemistry, urinalysis parameters and adverse event (AE) monitoring at baseline and end of 4-week treatment. At the end of 4-week treatment of TAPP-CZ nasal spray showed statistically and clinically significant improvement for overall RQLQ and four of its individual domain scores (namely activities, emotional, nasal symptoms, and eye symptoms), TNSS and NSS. Work productivity was significantly improved on 4-weeks of treatment by TAPP-CZ nasal spray as compared with placebo. TAPP-CZ was found to have excellent safety and tolerability profile with no serious AEs. In conclusion, TAPP-CZ nasal spray was found to be a useful treatment in management of acute seasonal AR patients.

* *Corresponding author*. Tel.: +91 20 6478 5063/64; fax: +91 20 2685 0039.
E-mail addresses: prasad@indusbiotech.com, prasad.thakurdesai@gmail.com (P.A. Thakurdesai).
2210-8033/$ – see front matter © 2014 Elsevier GmbH. All rights reserved.
http://dx.doi.org/10.1016/j.hermed.2013.12.002

1. Introduction

Allergic rhinitis (AR) is a common IgE-mediated inflammatory immune disease of the nasal mucosal membrane, affecting 500 million individuals worldwide. Allergic rhinitis (AR) is a highly prevalent allergic disease and also counts among the 10 most frequent reasons for a medical consultation (de la Hoz Caballer et al., 2012; Meltzer, 2007). AR is an inflammation of the nasal passages, usually with three cardinal symptoms namely, sneezing, nasal obstruction and mucous discharge with nasal itching. AR is hypersensitivity of nasal mucosa after allergen exposure due to an IgE-mediated inflammation of the membranes lining the nose (Lee et al., 2007). The prevalence of allergic rhinitis may vary in different countries due to the presence of different allergens; however, it has increased in the last two decades. AR can be classified as seasonal (intermittent) or persistent (perennial) based on frequency of attacks. AR is also classified as moderate or severe based on symptoms and quality of life (Bousquet et al., 2008). Allergic rhinitis has a significant negative impact on quality of life, mood, work performance and exacerbation of other medical conditions such as asthma and sinusitis (Gaga et al., 2000; Nathan, 2007).

Pharmacotherapy of AR is multifactorial as many interactive pathways are involved in its pathophysiology. Therefore, multi-directional treatment regimens such as allergen avoidance, symptomatic treatment and allergen immunotherapy have been used to control allergic responses (Nasser et al., 2008; Nouri-Aria, 2008). To target different symptoms, the class of drugs such as antihistamines, corticosteroids, mast cell stabilizers, decongestants, anti-leukotrienes and anticholinergics have been used (Al Suleimani and Walker, 2007; Leung and Hon, 2008). Although combination formulas containing antihistamines, decongestants and/or analgesics are sold over-the-counter (OTC) in large quantities for the common cold, the evidence of effectiveness is limited. Moreover, they are associated with adverse effects which limit their use. Therefore a search for novel agents in the treatment of AR is always ongoing. Medicinal plants and their bioactive compounds may provide a possible breakthrough in the treatment of AR.

Dietary polyphenols are reported to offer benefits in the management of many allergic disorders (Akazome, 2004; Bravo, 1998; Enomoto et al., 2006; Kojima et al., 2000). Cinnamon (*Cinnamomum zeylanicum* Syn *C. verum*, family: Lauraceae) bark polyphenol extract (CPE) has shown potential in the management of immune inflammation such as AR. Cinnamon bark widely used as a spice and flavorings agent, is native to Sri Lanka, Mayanmar (Burma) and the southern coastal strip of India. Being readily available as a food constituent, it also has a long history of traditional medicinal use in India, Sri Lanka, China, Egypt and European countries for many conditions including autoimmune (Kirtikar et al., 1975; Warrier et al., 1993) and inflammatory disorders (Khory and Katrak, 1903; Kirtikar et al., 1975; Warrier et al., 1993). Moreover, cinnamon bark is a certified GRAS (generally recognized as safe) ingredient in the USA.

Type-A proanthocynidins (TAPP) from cinnamon bark have been well-characterized components of CPE and thought to be responsible for many biological activities (Anderson et al., 2004). Proanthocyanidins are a combination of biologically active polyphenolic flavonoids including oligomeric proanthocyanidins that consist of a series of trimers and tetramer of flavan-3-ols, each with an A-type linkage (Anderson et al., 2004). Previous reports of immunomodulatory (Ravindran et al., 2004), anti-inflammatory (Cao et al., 2008; Cao and Anderson, 2011; Warrier et al., 1993), anti-arthritic (Joshi et al., 2001) and anti-viral (Shan et al., 2007) activities of TAPP from cinnamon bark further supports medicinal potential of TAPP in the management of immune inflammatory disorders such as AR.

Clinical, epidemiological and pathophysiological studies suggest a strong functional and immunological relationship between asthma and AR (Cruz et al., 2007; Feng et al., 2012; Palma-Carlos et al., 2001; Pawankar et al., 2012). Both AR and asthma have similar cellular responses, the inflammatory cascade and eosinophil infiltration of the nasal and bronchial epithelium exhibit different symptoms based on the differences in the physical structures involved (Kim et al., 2008). Furthermore, AR is implicated as one of the multiple risk factors for asthma development (Cruz et al., 2007). Recently, we have demonstrated ameliorative effects of TAPP based standardized extract of cinnamon bark (TAPP-CZ) in well-validated animal models of AR (Kandhare et al., 2013a) and asthma (Kandhare et al., 2013b). The present study was undertaken with the object of evaluating the efficacy and safety of TAPP-CZ in patients with seasonal allergic rhinitis.

Both topical (e.g. nasal) and systemic (e.g. oral) agents are found to be equally efficacious formulations against AR. However, topical formulations are preferred over systemic administration. Nasal formulations have been found to be better in terms of efficacy, tolerability, and patient preference and adherence and so considered for first-line treatment for AR. For example, nasal spray formulation of corticosteroids is more strongly recommended than systemic formulation due to lesser side effects (Karaki et al., 2012). Therefore, the present study was designed to evaluate efficacy and safety of TAPP-CZ nasal spray in patients with seasonal AR.

Although not a life threatening disease, AR is known to deleteriously affect quality of life by causing fatigue, headache, cognitive impairment and other associated symptoms (Wallace et al., 2008). The Juniper rhinitis quality of life questionnaire (RQLQ) is a validated tool for assessing quality of life in allergic rhinitis (Juniper and Guyatt, 1991; Juniper, 1997). In previous studies this outcome has shown strong evidence for reproducible therapeutic effects and there are established data on which to base power calculations and clinically significant changes for definitions of equivalence or non-inferiority limits. It is based on the impact of symptoms for individuals and thus meets the criteria for efficacy assessment of AR.

Therefore, the present study was conducted as a double blind, placebo controlled proof-of-concept study to evaluate the efficacy and safety of TAPP-CZ as a nasal spray in seasonal AR patients with special reference to quality of life measurement (RQLQ) and nasal symptoms (obstructions, drainage, itch and sneezing).