1. INTRODUCTION

Since ancient times man has used various natural materials as a source of medicines. Plants always had an important role to play in medicine and public health. The knowledge for the use of medicinal plants and their properties was acquired by means of trial & error and transmitted from generation to generation (Ghorbani, 2005). Medicinal folklore over the years has proved to be an invaluable guide in present day screening of drugs. In recent years, interest in ethno-botany has increased dramatically; also use of ethno-botanical information in medicinal plant research has gained considerable attention in segments of the scientific community (Heinrich, 2000).

*Achillea millefolium* Linn belonging to family Compositae is a widely distributed medicinal plant throughout the world and has been used since ancient times. Popular indications of this plant include treatment of wounds, bleedings, headache, inflammation, rheumatic pains, spasmodic diseases, flatulence and dyspepsia. Various effects of these plants may be due to the presence of a broad range of secondary active metabolites such as flavonoids, phenolic acids, coumarins, terpenoids (monoterpenes, sesquiterpenes, diterpenes, triterpenes) and sterols which have been frequently reported from *Achillea* species (Saeidnia *et al*., 2011).

*Rubia cordifolia* Linn belonging to family Rubiaceae is a well-known ayurvedic herb popularly known as Indian Manjit. Roots are traditionally used as anti-inflammatory, astringent, tonic, antiseptic, deobstruent, anti-dysenteric, blood purifier. In the Cape Province, natives take a decoction of the leaf or root for pleurisy and other inflammatory conditions of the chest. This plant is an important ingredient of many ayurvedic preparations. Isolation and identification of various chemical constituents like anthraquinones, iridoid glycoside, naphthoic acid esters, bicyclic hexapeptides, and triterpenes have been carried out from *Rubia cordifolia* Linn (Deshkar *et al*., 2008).

*Saussurea costus* (Falc.) Lipschitz, syn *Saussurea lappa* C.B. Clarke (Compositae) is a well-known and important medicinal plant widely used in several indigenous systems of medicine for the treatment of various ailments, viz. asthma, inflammatory diseases and stomach problems. Sesquiterpene lactones have been reported as the major phytocstituents of this species. A number of different pharmacological experiments in a number of *in vitro* and *in vivo* models have convincingly demonstrated
the ability of *Saussurea costus* to exhibit anti-inflammatory, anti-ulcer, anticancer and hepatoprotective activities, lending support to the rationale behind several of its traditional uses. Costunolide, dehydrocostus lactone and cynaropicrin, isolated from this plant, have been identified to have potential to be developed as bioactive molecules. Due to the remarkable biological activity of *Saussurea costus* and its constituents it will be appropriate to develop them as a medicine (Pandey *et al.*, 2007). Extensive search had been carried out on scientific research data of *A. mililfolium*, *R. cordifolia* and *S. lappa* which revealed that, all of these plants traditionally used for anti-inflammatory indications have the ability to suppress the biochemical markers of inflammation. Phytochemical investigation of these plants showed that the biological active principles present in these are mainly terpenoids and glycosides. It is well established that various plant-originated constituents such as glycosides, flavonoids and terpenoids significantly inhibited asthmatic responses (Jang *et al.*, 2010). In the present study, we isolated bioactive constituents, namely achillicin, chamazulene, rubiadin, mollugin, costunolide, dehydrocostus lactone and cynaropicrin, responsible for anti-inflammatory property from these plants and evaluated for anti-asthmatic activity.

Asthma is a chronic disorder in which the airways are characterized by inflammation, hyperresponsiveness, and intermittent obstruction. In the recent years, the morbidity and mortality of population due to asthma is increasing despite the advances being made in understanding of this disease and availability of improved medications and information on treatment (Shabaraya *et al.*, 2008). As per WHO, currently there are approximately 300 million people currently suffering from asthma globally (a number that could increase by further 100 million by 2025) and approximately 255,000 people died because of asthma every year (Aggarwal *et al.*, 2006; Jindal, 2007; WHO, 2011). As per National family health survey of India, 2468 persons per 100,000 population are reported to be suffering from asthma, which is considerably higher in rural areas (2649 per 100,000 population) than in urban areas (1966 per 100,000 population) (MHFW, 2009). Although the fundamental causes of asthma are not completely understood, numerous antigens or allergens are capable of triggering the acute attacks of asthma. However, for symptomatic relief medical practitioners prescribe β₂ adrenergic receptor agonists, glucocorticoids, leukotriene receptor antagonists, leukotriene synthesis
inhibitors, anti-IgE therapy, cromones, xanthines and anticholinergic agents. These treatments have their own limitations which can be their cost of treatment or their deleterious side effects *viz.* insomnia, anxiety, cardiotoxicity, hypertension, tachycardia, tremor, palpitations, immunodeficiency, hyperglycemia, increased skin fragility and negative calcium balance (Waldeck, 2002).

The pathophysiology of asthma reveals that the main etiological factors are inflammation and immunomodulation. Inflammation can be caused by degranulation of mast cells which results in the release of an array of cytokines (Borish and Joseph, 1992) via exposure of ova allergen to antigen-presenting cells (macrophages, dendritic cells and B cells) or Th2 mediated cytokine or reactive oxygen species (free radicals) which leads to injury of epithelial tissue of airways. Immunomodulation occurs due to formation IgE via B cells. In aetiology of asthma, chemokine (PAF, TNFα), interleukins (IL-6, IL-8), nitric oxide (NO) and oxidative stress (SOD, EPO) plays a major role. PAF, released by mast cells and eosinophil, directly act on airway smooth muscle and lead to bronchoconstriction. Apart from this PAF and TNFα is a pro-inflammatory cytokines, causes chemotaxis, recruitment of inflammatory cells and release of no of inflammatory mediators. Furthermore, free radical generates and leads to oxidative burst. Interleukins such as IL-6 and IL-8 plays a major role in pathogenesis of asthma. IL-6 contributes to both disease severity and progression (Smolen et al., 2008), released from various inflammatory cells, fibroblasts and erythropoietic cells. IL-6 could also influence lung physiology by promoting an increase in airway wall thickness, sub-epithelial fibrosis, and smooth muscle hypertrophy & proliferation (Qiu et al., 2004). IL-8 takes role in the activation of neutrophils and is a potent chemoattractant of neutrophils during the airway inflammation (Nocker et al., 1996), release by neutrophils and airway epithelial cells by activation via TNFα, a putatively important cytokine in mediating allergic airway inflammation. Likewise, on progression of inflammation, further oxidative load increased due to infiltration of inflammatory cells, leads to eosinophilia.

In view of all these factors, the present study was an attempt to evaluate the potential role of isolated compounds from *A. millefolium*, *R. cordifolia* and *S. lappa*, which have anti-inflammatory, anti-oxidant, nitric oxide and immunomodulating efficiency in the management of asthma in ovalbumin induced rat model.