Chapter 3
Review of literature
3.1 Treatments for inflammation

Current treatment against inflammation includes use of Steroids and Non Steroidal Anti-inflammatory Drugs (NSAIDs) (Conforti et al., 2008). Three major activities due to which NSAIDs have been used very commonly for the inflammatory disorders are anti-inflammatory, anti-pyretic and analgesic activity. Commonly used NSAIDs are phenylbutazone, diclofenac and meloxicam (Modi et al., 2012).

NSAIDs produce their therapeutic effects by inhibiting by inhibiting the activities of enzyme Cyclooxygenases (COX) (Vane et al., 1998; Modi et al., 2012). Cyclooxygenases (COX) are the enzymes that mediate the production of prostaglandins and thromboxane from arachidonic acid (a dietary fatty acid). COX-1 is constitutive enzyme plays an important role in maintaining renal and gastrointestinal blood flow as well as ensuring platelet integrity, while COX-2, an inducible form of the enzyme is up-regulated in inflammatory disease conditions (Bergh and Budsberg, 2005). Older NSAIDs (e.g. Ibuprofen) inhibits COX-1 which in turn leads to various adverse effects like gastrointestinal (GI) disturbances; whereas, newer NSAIDs (e.g. Celecoxib, Valdecoxib, Rofecoxib, etc.) inhibit COX-2, thereby decreasing the adverse effects. Inhibiton of COX-1 by older NSAIDs e.g. Ibuprofen leads to various adverse effects like gastrointestinal (GI) disturbances. Whereas, newer NSAIDs e.g. Celecoxib, Valdecoxib, Rofecoxib, etc. inhibit COX-2, thereby decreasing the adverse effects. But this selectivity of COX inhibition may be lost in case of overdose or prolonged use of the drug, which results in adverse effects (Rainsford, 2007).

Therefore, along with their anti-inflammatory, analgesic and antipyretic activities, prolonged use of NSAIDs in large doses, causes GI Tract related problems (including ulceration, obstruction and hemorrhage), cardiovascular risks, blood clotting and renal problems, etc. (Patwardhan et al., 2005; Conforti et al., 2008; Modi et al., 2012).
3.1.1 Cervicitis

As the term cervicitis is reserved to the inflammatory condition of the endocervix including the glands and the stroma, which may be with or without infection (Bhandari et al., 2000; Cohen et al., 2002; Manhart et al., 2003; Ness et al., 2004; Falk et al., 2004; Falk et al., 2005; Marrazzo et al., 2006). Since a range of infectious as well as non-infectious causes are responsible for cervicitis, the treatments for cervicitis differ accordingly. Table 2 represents the available treatments on the basis of causative factor (Wilson et al., 2009).

To invent a treatment without any side effects is one of the many hurdles that need to be overcome by new developing drugs. Thus, it becomes important to identify alternative drugs that can play a significant role in treatment of inflammatory conditions without imparting side effects or with minimum side effects.

The use of natural remedies has a long traditional history with minimum or no side effects. Since ages, there is exclusive use of plants as drugs in traditional medicines representing a large source of natural medicines. They are also known to play a crucial role in management of various inflammatory diseases; therefore, naturally originated agents with such medicinal potential are enviable to surrogate the use of chemical therapeutics (Conforti et al., 2008). The classical example to treat Inflammation and or cervicitis is *Dashamoola* (Anonymous, 1990; Jagtap et al., 2009).
<table>
<thead>
<tr>
<th>Causative agent</th>
<th>Drug for treatment</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candida</td>
<td>Nystatin (cream and suppository)</td>
<td>Local irritation. Yeast balanitis may occur in male partners.</td>
</tr>
<tr>
<td></td>
<td>Fluconazole</td>
<td>GI upset. Contraindicated in pregnancy. Cytochrome P450 inhibitor, so consider drug interactions.</td>
</tr>
<tr>
<td><em>Trichomonas</em></td>
<td>Metronidazole</td>
<td>GI upset, metallic taste, peripheral neuropathy, dizziness; disulfiram-like reaction is possible. Resistant strains of <em>Trichomonas</em> can occur and are usually cured with increased doses. Category B in pregnancy.</td>
</tr>
<tr>
<td>Bacterial infections</td>
<td>Metronidazole gel</td>
<td>Can cause vaginal candidiasis.</td>
</tr>
<tr>
<td></td>
<td>Clindamycin</td>
<td>Colitis. Category B in pregnancy.</td>
</tr>
<tr>
<td></td>
<td>Clindamycin 2% cream</td>
<td>Vaginal yeast infections. Category B in pregnancy.</td>
</tr>
<tr>
<td></td>
<td>Clindamycin ovules</td>
<td>Vaginal yeast infections. Category B in pregnancy.</td>
</tr>
<tr>
<td></td>
<td>Tinidazole</td>
<td>GI upset, but may be less than with metronidazole. Contraindicated in first trimester of pregnancy.</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>Ceftriaxone</td>
<td>Category B in pregnancy. Always combine with chlamydia treatment unless a DNA amplification test fails to detect chlamydia.</td>
</tr>
<tr>
<td></td>
<td>Cefixime</td>
<td>Category B in pregnancy.</td>
</tr>
<tr>
<td></td>
<td>Spectinomycin</td>
<td>Local pain at injection site.</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>Doxycycline</td>
<td>GI upset. Photosensitivity. Compliance may be a problem. Contraindicated in pregnancy.</td>
</tr>
<tr>
<td></td>
<td>Erythromycin</td>
<td>GI upset. Compliance may be a problem. Category B in pregnancy.</td>
</tr>
<tr>
<td></td>
<td>Azithromycin</td>
<td>GI upset possible, including nausea, vomiting, abdominal pain, and diarrhea. Expensive. Category B in pregnancy.</td>
</tr>
</tbody>
</table>

Category B: There is no evidence of risk in humans, but controlled studies are not available. GI: Gastro Intestinal
3.2  **Dashamoola**

According to the Ayurvedic Pharmacopoeia of India (Anonymous, 1990), *Dashamoola*, one of the folk medicines, is a polyherbal formulation believed to have the potential for providing relief from inflammation. Roots of plants used in *Dashamoola*, either singly or in combination, have always been an integral part of treatment of various ailments in *Ayurveda* as well as in traditional medicines of diverse communities across India. Pawra tribes from Satpura hills of Maharashtra routinely use these individual plants to treat the inflammatory condition (Jagtap et al., 2009).

Following subsection describe ethnobotanical and ayurvedic uses of dashamoola plants and their pharmaceutical properties as well as phytochemical characters.

### 3.2.1 *Aegle marmelos* (L.) Corr.

**Ethnobotanical uses:** Various plant parts of *A. marmelos* such as leaves, fruits, stem and roots are used in treatment of several ailments. Decoction of root and root bark is also known to be useful in intermittent fever, hypo-chondriasis, melancholia and palpitation of the heart (Nadkarni, 2000). Root bark of *A. marmelos* is used as a fish poison, anti dog bite, melancholia, etc. It is also used to treat gastric troubles, heart disorders, fever, antiamoebic, hypoglycemic, rheumatism, hypo-chondriasis, malaria, jaundice, and skin diseases such as ulcers, urticaria, and eczema (Kirtikar and Basu, 1935; Brijesh et al., 2009; Patel et al., 2012). Roots of *A. marmelos* have been used in ethno medicines for its several medicinal properties like astringent, demulcent, antipyretic, aphrodisiac, as an antidote to snake venom, vomiting, etc. (Veerappan et al., 2000; Khare, 2004a; Mazumder et al., 2006; Sukumaran and Raj, 2010; Patel et al., 2012).

**Ayurvedic uses:** According to API, roots of *A. marmelos* are used for the Vatavyadhi, Sotha, Sula, Agnimandya, Chardi, Mutrakrcchra, and Amavata (Anonymous, 1990). Its roots are also used to treat arthritis (Subramoniam et al., 2013).

**Pharmacological activities:** Root extracts are reported to have anti-inflammatory and wound healing properties (Kirtikar and Basu, 1935; Jaswanth et al., 2001; Trease and Evans, 2003; Hari and Lakshmi, 2012). Alcoholic extracts of the roots showed hypoglycemic and antidiabetic activity (Karunanayake et al., 1984; Sabu and Kuttan, 2004; Ravi et al., 2009). The root extracts also possess anti-oxidant activity.
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(Bramhachari et al., 2010). The aqueous root bark extract have shown anti-inflammatory activity in carrageenan induced paw edema and cotton pellet induced granuloma models (Benni et al., 2011).

**Phytochemical studies:** Marmin, a compound isolated from roots of *A. marmelos* have showed anti-inflammatory activity in carrageenan induced paw edema in rats (Pitre and Srivastava, 1987). Several chemical constituents like Alkaloid, Halopine, Coumarins (marmin, marmesin, scoparone, scopoletin, umbelliferone, umbelliferine psoralen, marmelide, xanthotoxol, impertoin and skimmiane), polysaccharides (psoralin, xanthotoxin and scopolotein) and Terpines have been extracted from roots (Farooq, 2005; Sharma et al., 2006; Patel et al., 2012; Yadav et al., 2015) and showed to possess anti-fungal activity (Rana et al., 1997; Patil et al, 2004) and anti thyroid activity (Panda and Kar, 2006).

3.2.2 *Desmodium gangeticum* (L.) DC.

**Ethnobotanical uses:** Ethnomedicinal surveys have mentioned use of *D. gangeticum* for toothache, asthma bronchitis, diarrhea, dysentery, fever, mouth ulcer, typhoid, cough, vomiting, rheumatism, as antidote in snake bite, sedative agent and medicine for abortion, to cure premature ejaculation, etc. (Kirtikar and Basu, 1999a; Jain et al., 2005; Chakraborty and Bhattacharjee, 2006; Tayade and Patil, 2006; Badgujar et al., 2008; Jeyaprakash et al., 2011; Ma et al., 2011; Rastogi et al., 2011).

**Ayurvedic uses:** In Ayurveda, roots of *D. gangeticum* are used for Jvara, Meha, Arsa, Chardi, Sopha, Svasa, Kasahara, Krmi, Rajayaksma, Netra Roga, Hrdaya Roga, Raktagata Vata, Vata Ardhvabhedaka, Mudha Garbha (Anonymous, 1990). The roots are also used in polyherbal formulations to treat arthritis (Subramoniam et al., 2013).

**Pharmacological activities:** Aqueous extract of root of *D. gangeticum* has been shown to have hypocholesterolemic and antioxidant effects in isoproterenol induced myocardial infraction (Govindarajan et al., 2003). Rathi et al, (2004) studied the water decoction of root for anti-inflammatory, anti-nociceptive activity in experimental animals. Ethanolic extract of root was studied for various acute and chronic ulcers in mouse models, in which it significantly decreased the ulcer index and lesion number against ethanol induced acute gastric ulcer in mice (Mahesh et al., 2012). Aqueous extract of roots have also shown anti-arthritic activity *in vitro* (Vedpal et al., 2013).

**Phytochemical studies:** Gangetin, a compound from hexane extract of *D. gangeticum*, showed significant anti-inflammatory activity in carrageenan induced edema,
granuloma pouch, cotton pellet granuloma and formaldehyde induced arthritis in rat models (Ghosh and Anandkumar, 1983). Other bioactive compounds isolated from roots of *D. gangeticum*, include $7\alpha,12\alpha$-dihydro-13methoxy-3,3-dimethyl-11-(3-methyl-2-butenyl)-3H,7Hbenzofuro[3,2-C]pyrano[3,2-g]benzopyran-10-ol, Gangetinin, Desmodin, 3,4-dihydroxy benzoic acid (Protocatechuic acid) (Ganjhu et al., 2014).

### 3.2.3 *Gmelina arborea* Roxb.

**Ethnobotanical uses:** Traditionally, roots of *G. arborea* are used as demulcent, lactagogue, refrigerant, stomachic, galactogogue, laxative, anthelmintic, anti-inflammatory, tonic, anthelmintic, hyperdipsia, leucorrhoea, colitis, trichogeneous, leprosy, anemia, strangury and skin disease. The root decoction is also used for abdominal tumors (Nadkarni, 1976; Kirtikar and Basu, 1984; Warrier et al., 1995; Banu et al., 2013). It is also used for urinary discharges and strangury, piles, washing and healing of septic wounds, wound healing, as antidote in scorpion sting, etc. (Shirwaikar and Somashekar, 2003; Jain et al., 2005; Ignacimuthu et al., 2006; Punjani, 2010; Panda et al., 2011; Korpenwar, 2012).

**Ayurvedic uses:** In Ayurvedic literature it is mentioned that, roots of *G. arborea* are used for Jvara, Trsna, Daha, Arsa, Sotha (Anonymous, 1990). Roots of this plant are used in polyherbal formulations to treat arthritis (Subramoniam et al., 2013).

**Pharmacological activities:** Methanol extract of root and ethyl acetate fraction of *G. arborea* showed immune stimulant activity in humoral and cell-mediated immune response in animal models (Shukla et al., 2010). Methanol extract of roots was also found to possess anti-fertility effects in Albino mice (Kalita et al., 2011). Aqueous and methanol extracts of *G. arborea* showed anti-inflammatory activity in carrageenan induced inflammation in rat model and anti-nociceptive activity by using hot plate test and writhing test in Swiss albino mice (Kulkarni et al., 2013). The petroleum ether extract of roots was found to possess the laxative activity, whereas ethanol and petroleum ether extract exhibited antipyretic activity in wistar rats (Panda et al., 2015).

**Phytochemical studies:** Roots of *G. arborea* are reported to contain umbelliferone 7-apiosylglucoside, arboreol, gmelanone ceryl alcohol, gmelfuran, gmelinol, hentriacontanol-I, n-octacosanol, β-sitosterol, sesquiterpene, etc. (Govindachari et al., 1972; Row et al., 1974; Satyanarayana et al., 1985).
3.2.4  *Oroxylum indicum* Vent.

**Ethnobotanical uses:** Traditionally, root bark is used in fever, bronchitis, intestinal worms, asthma, inflammation and for anal troubles, etc. (Kirtikar and Basu, 1987). Root paste is also used externally for wound healing (Sumner, 2000). Ethnomedicinal surveys showed that roots are used for diarrhoea, dysentery, burning maturation, jaundice, inflammation, rheumatism, stomach trouble, as antidote and abortifacient (Jain et al., 2005; Kunwar et al., 2009; Rout et al., 2009; Jamir et al., 2010; Choudhary et al., 2011).

**Ayurvedic uses:** In Ayurveda, roots are used for Vatatisara, Kasa, Aruci, Basti Roga, Amavata, Udara Roga, Urustambha, Vatavyadhi, Karna Roga and Sotha (Anonymous, 1990). Roots of this plant are used in polyherbal formulations to treat arthritis (Subramoniam et al., 2013).

**Pharmacological activities:** Dicloromethane extract of roots of *O. indicum* found to have anti-inflammatory properties (Ali et al., 1998). Ethyl acetate and Methanol extracts of *O. indicum* have found to possess antimicrobial activity (Uddin et al., 2003; Thatoi et al., 2008). Ethanol, Petroleum Ether and n-Butanol extracts have proven antiulcer activity (Khandhar et al., 2006), whereas n-Butanol extract showed Immunomodulatory potential (Zaveri et al., 2006). Alcoholic and n-Butanol extracts have also proven their gastroprotective effects in animal experiment (Zaveri and Jain, 2007). It has also shown gastroprotective effect in ethanol and WIRS-induced gastric ulcers in rats (Maitreyi and Jain, 2007). Methanol and water extracts have proven their anti-oxidant activities (Mishra et al., 2010b). n-butanol fraction of root bark of *O. indicum* showed significant anti-inflammatory activity in carrageenan-induced rat paw edema and cotton pellet-induced chronic inflammation in rats and analgesic activity in experimental animals (Zaveri and Jain, 2010). Aqueous root extract of *O. indicum* has shown potent hepatoprotective activity in paracetamol induced liver damage in rats (Sastry et al., 2011). Decoction of root has anti-inflammatory potential in carrageenan induced paw edema in rats (Doshi et al., 2012). Anti-arthritic activity of chloroform, ethyl acetate and n-butanol extracts root bark was evaluated against adjuvant-induced arthritis (Karnati et al., 2013).

**Phytochemical studies:** Root bark contains Ellagic acid, Baicalein (5,6,7-trihydroxyflavone), Oroxylin-A (5,7-Dihydroxy-6-methoxyflavone), Chrysin (5,7-dihydroxyflavone) (Subramanian and Nair, 1972; Vasanth et al., 1991; Grampurohit et al., 1994; Sharma et al., 2001; Dinda et al., 2007). Chrysin has found to possess...
anti-inflammatory activity (Ali et al., 1998). The quantification of Baicalein, Chrysin, Biochanin-A and Ellagic acid in root bark was carried out by RP-HPLC with UV detection method (Zaveri et al., 2008).

3.2.5 **Premna obtusifolia** R. Br.

**Ethnobotanical uses:** Decoction of root of *P. integrifolia* (*P. obtusifolia*) is cordial, stomachic, carminative, alterative, as a tonic, good for liver complaints, and also useful in urticaria (Otsuka et al., 1993). The decoction of roots of *P. obtusifolia* is used to treat gonorrhea (Rao et al., 1984), as an anti-parasitic agent (Desrivot et al., 2007), for cancer (George et al., 2008), and is also used for infectious disease (Tiuman et al., 2011).

**Ayurvedic uses:** Roots of *P. obtusifolia* are used in various inflammatory conditions like rheumatoid arthritis, rhinitis, and abscess. It is also suggested for Vatavyadhi, Prameha, Medoroga, Agnimandya (Kumari et al., 2011). It is used in polyherbal formulations to treat arthritis (Subramoniam et al., 2013).

**Pharmacological activities:** Methanolic extract of the roots have shown significant anti-inflammatory activity in carrageenan-induced rat hind paw edema, histamine induced wheal formation, and acetic acid-induced mouse vascular permeation (Gokani et al., 2011). Ethanol extract of roots of *P. serratifolia* (*P. obtusifolia*) were investigated against paracetamol induced oxidative stress and hepatotoxicity in blood and liver of male albino rats and found to possess hepatoprotective and anti-oxidant activity (Singh et al., 2011). Root and root callus extracts of *Premna serratifolia* L. augmented to have good anti-inflammatory activity against carrageenan induced paw edema (Singh et al., 2012). Decoction of roots of *P. integrifolia* has shown anti-inflammatory activity in carrageenan induced rat paw edema model (Kumar et al., 2015).

**Phytochemical studies:** The root has been reported to contain an alkaloid premnazole, which is a proven anti-inflammatory agent (Barik et al., 1992). Various other compounds have been isolated from roots of *P. obtusifolia* such as Pimarane I, Pimarane II, Rosane, Abietane I, Abietane II, Abietane III, Abietane IV, 6α-Hydroxy-5,6-dihydrosalviaperanol, 6-Hydroxysalvinolone, Obtusinones D, Obtusinones E, 11,12-Dihydroxy-10,6,8,11,13-icetexapentan-1-one (Salae et al., 2009; Asik et al., 2010; Abdul et al., 2011; Salae et al., 2012, 2013). The antioxidant activity and active principle of the root woody tissues were investigated from *Premna serratifolia* Linn.
(syn: *Premna integrifolia*, *Premna obtusifolia* R. Br.), the isolated active antioxidant principle was identified as acteoside (verbacoside) by spectroscopy studies. Acteoside was found to be more active than the crude root wood extract and therefore assumed to be responsible for most of the reported pharmacological activities of the plant (Bose et al., 2013).

### 3.2.6 *Solanum anguivi* Lam.

**Ethnobotanical uses:** In ethno medicine, roots of *S. anguivi* are used for asthma, toothache, dry cough, bronchitis, leprosy, colic, blackleg, anthrax, disuria, chronic fever, alopecia, dropsy, jaundice and haematuria (Negi et al., 2002; Dhiman, 2005; Ishtiaq and Khan, 2008; Sikdar and Dutta, 2008; Mesfin et al., 2009; Nath and Khatri, 2010; Singh et al., 2010).

**Ayurvedic uses:** *S. anguivi* roots are used for Hrdroga, Jvara, Svasa, Sula, Agnimandya in Ayurveda (Anonymous, 1990). It is one of the ingredients of kashayas in Ayurveda, Mohaamanjishtaadi and Panchathikthakam, which is used as a therapy for arthritis and related diseases. It is also used for the treatment of rheumatoid arthritis, chronic skin diseases, anaemia, paralytic conditions, filariasis, ophthalmic diseases and obesity (Subramoniam et al., 2013).

**Pharmacological activities:** Ethanol extract of roots of *Solanum indicum* (*S. anguivi*) have shown anti-inflammatory activity in carrageenan induced rat paw edema model (Singh et al., 1998).

**Phytochemical studies:** It has been reported that roots of this plant contains wax, fatty acids, alkaloid solanine and solanidine, disogenin, lanosterol, β-sitosterol, solasornine, solamargine and solasidine (Deb et al., 2014).
3.2.7  *Solanum virginianum* L.

**Ethnobotanical uses:** In ethno medicine, roots of *S. virginianum* are used for cough, gum pain, tooth-ache, asthma, boils, chest pain and against small pox (Tayade and Patil, 2006; Das et al., 2008; Sikdar and Dutta, 2008; Rajakumar and Shivanna, 2009; Jain and Singh, 2010).

**Ayurvedic uses:** In Ayurveda, whole plant of *S. surattense* (*S. virginianum*) is used for Svasa, Kasa, Jvara, Aruci, Pinasa, Parsvasula, Svarabheda (Anonymous, 1990). It is one of the ingredients of kashayas in Ayurveda, Mohaamanjishtaadi, which is used as a therapy for arthritis and related diseases. It is also used for the treatment of rheumatoid arthritis, chronic skin diseases, anaemia, paralytic conditions, filariasis, ophthalmic diseases and obesity (Subramoniam et al., 2013).

**Pharmacological activities:** Root extract of *S. surattense* have shown *in vitro* antioxidant activity and found to contain enzymic antioxidants such as catalase, superoxide dismutase, glutathione reductase, glutathione S-transferase and glutathione peroxidase, and non enzymic antioxidants such as ascorbic acid, α-tocopherol, reduced glutathione, flavonoids and carotenoids (Priyadarsini et al., 2010). Ethyl acetate, chloroform and ethyl alcohol fractions of roots of *S. xanthocarpum* (*S. virginianum*) were found to posses free radical scavenging activity in DPPH radical scavenging assay and lipid peroxidation inhibition in rat liver homogenate (Kumar et al., 2012). Ethanolic, ethyl acetate and aqueous fractions of roots of *S. xanthocarpum* have found to posses anti-oxidant activity in reducing power assay and lipo-protective activity in lipid peroxidation inhibition assays in rat kidney tissue *in vitro* (Kumar and Pandey, 2012). Carbon tetrachloride, chloroform, ethanolic and hexane extracts of root of *S. xanthocarpum* possess antimicrobial and antipyretic activities. Whereas, ethanolic and chloroform extracts showed anti-inflammatory activity *in vitro* (Patil and Wadhawa, 2013). Carbon tetrachloride, chloroform, ethanolic and hexane extracts of the root of *Solanum xanthocarpum* were studied for antimicrobial and antipyretic activities. It has anti-inflammatory and antioxidant activity for ethanolic and chloroform extract (Patil and Wadhawa, 2013).

**Phytochemical studies:** Root extract of *S. surrattense* contains alkaloids, carbohydrates, proteins, resins, saponins, steroid, tannin, starch, glycosides, flavonoids and triterpenoids (Kumar et al., 2012; Ghildiyal and Joshi, 2014; Archana and Jessy, 2015).
3.2.8 *Stereospermum colais* Mabb.

**Ethnobotanical uses:** The roots of *S. colais* are diuretic, lithotrophic, expectorant, cardio tonic, aphrodisiac, anti-inflammatory, anti-bacterial, febrifuge, tonic, anti-emetic and anti-pyretic (Kirtikar and Basu, 1999b; Warrier et al., 2002). The decoction of root is used in asthma and cough (Warrier et al., 2002; Meena et al., 2010). In ethno medicine, roots are used to regularize menstrual disorders and for curing nervous disorders (Jain et al., 2005; Rout et al., 2009).

**Ayurvedic uses:** In Ayurveda, roots of *S. chelenoides* (*S. colais*) are used for Svasa, Sotha, Arsa, Chardi, Hikka, Trsa, Amlapitta, Rakta Vikara, Mutravikara, Agnidadha, Vrana Ruja, Visphota and Medoroga (Anonymous, 1990). Roots of this plant are also used in polyherbal formulations to treat arthritis (Subramoniam et al., 2013).

**Pharmacological activities:** Aqueous extract of root bark of *Stereospermum suaveolens* DC. (*S. colais*) has shown anti-inflammatory effects in carrageenan-induced paw edema model (Kharat et al., 2012). Acetone and methanol extracts of *S. colais* roots have shown antidiabetic, antiperoxidation, xanthine oxidase inhibition and radical scavenging activities *in vitro* (Rani and Padmakumari, 2012). Ethanolic extract of *S. colais* was studied *in vitro* in protein denaturation method using bovine serum albumin and found to posses antiarthritic activity (Latha et al., 2015).

**Phytochemical studies:** Root contains α-sitosterol, n-triacontanol, lapachol, dehydro α-lapachone and dehydrotectanol (Yoganarasimhan, 2000).

3.2.9 *Tribulus terrestris* L.

**Ethnobotanical studies:** In ethno medicine roots of *T. terrestris* are used for male weakness, to prevent white discharge in women, in strangury, to treat urinary troubles and to help in expelling kidney stones (Muthu et al., 2006; Chauhan et al., 2009; Punjani, 2010; Singh et al., 2010; Francis et al., 2011; Ma et al., 2011). It is also used in type II diabetes mellitus (Akram, 2013).

**Ayurvedic studies:** Roots are used for Sularoga, Hrdroga, Vataroga, Mutrakrcchra, Asmari, Kasa and Svasa (Anonymous, 1990). Roots are one of the ingredients of kashayas in Ayurveda, Raasnasapthakam, which is used as a therapy for rheumatoid arthritis (Subramoniam et al., 2013).

**Pharmacological activities:** Aqueous extract of root of *T. terrestris* have shown antimicrobial activity against 11 species of pathogenic and non-pathogenic microorganisms (Al-Bayati and Al-Mola, 2008). The methanol extract of whole plant
showed anti-inflammatory activity in Carrageenan induced inflammation in rats and antimicrobial activity against Gram (+) and Gram (-) bacteria (Baburao et al., 2009). The radiomodulatory influence of root extract was observed against radiation induced alterations in Swiss albino mice (Kumar et al., 2009).

**Phytochemical studies:** Roots contains steroidal saponins, alkaloids, lignanamides, carbohydrates and flavonoids (Deepak et al., 2002).

### 3.2.10 *Uraria picta* (Jacq.) Desv. ex DC.

**Ethnobotanical uses:** *U. picta* roots are used traditionally for dysentery, sore mouth, snake bite and as abortifacient (Chakraborty and Bhattacharjee, 2006; Jain and Singh, 2010; Shukla and Chakravarty, 2010).

**Ayurvedic uses:** Roots of this plant are used as Sangrahika, Vatahara, Tridoshaghna, Vrushya, Sara, Dahahara, Jwarahara, Shwasahara, Raktatisarahara, Trut hara, Vamihara (Bhavamisra, 2013).

**Pharmacological activities:** Ethanolic extract of whole plant of *U. picta* have shown inhibitory activity in NO radical scavenging assay and lipoxygenase assay *in vitro*; and anti-inflammatory activity *in vivo* in carrageenan induced rat paw edema (Ahirrao et al., 2007).

**Phytochemical studies:** Isoflavanones, triterpenes and steroids were isolated from the roots of *U. picta* and studied for their anti-microbial activity (Rahman et al., 2007).
3.3 Additional plants

3.3.1 Asparagus racemosus Willd.

Ethnobotanical uses: Traditionally roots of *A. racemosus* are used in nervous disorders, dyspepsia, diarrhoea, dysentry, tumors, inflammations, hyperdipsia, neuropathy, hepatopathy, cough, bronchitis, hyperacidity and certain infectious diseases (Sharma et al., 2000). It is also used in problems related with menstruation, female infertility, menopause, mammary carcinoma and as a post partum tonic (Khulbe, 2015).


Pharmacological activities: Methanolic extract of culture of roots (*in vitro*) of *A. racemosus* have shown anti-inflammatory activity in carrageenan induced rat paw edema model (Asmari et al., 2004). Crude hydro-alcoholic extract and its four fractions (methanol, ethyl acetate, n-Butanol and precipitated aqueous) have shown to posses anti-oxidant activity and hepatoprotective activity (Acharya et al., 2012). Decoction of roots has proven its anti-inflammatory activity in carrageenen induced rat paw edema model (Joshi and Thatte, 2012). Ethanolic extract of root revealed antibacterial activity against *Staphylococcus aureus*, *Bacillus subtilis*, *Staphylococcus werneri*, *Pseudomonas putida*, *Pseudomonas aeruginosa* and *Proteus mirabilis* (Ravishankar et al., 2012). Ethanolic extract of *A. racemosus* root showed anti-inflammatory and anti-arthritic activity in carrageenan induced rat paw edema and Complete Freund’s Adjuvant induced arthritis in rat models respectively (Mittal and Dixit, 2013a). Hydroalcoholic extract of roots have shown anti-inflammatory and anti-arthritic activity in carrageenan induced paw edema model and Freund’s Complete adjuvant induced arthritis model respectively (Mittal and Dixit, 2013b). Antipyretic activity of aqueous and ethanol extract of root of *A. racemosus* was determined by brewer’s yeast induced pyrexia method, wherein ethanolic extract showed significant antipyretic effect compared to the aqueous extract (Vasundra and Divya, 2013).

Phytochemical studies: Racemofuran isolated from roots of *A. racemosus* has anti-oxidant activity (Wiboonpun et al. 2004). The major active constituents of roots include steroidal saponins (Shatavarins I-IV) (Mishra et al., 2013). Phytochemical
screening revealed the presence of alkaloids, carbohydrates, glycosides, phenolic compounds (ferulic acid, rutin, quercetin, kaempferol and flavonoids), tannins and flavonoids (Singh and Sinha, 2014).

### 3.3.2 *Curcuma longa* L.

**Ethnobotanical uses:** A paste of powdered rhizome of *C. longa* Linn. is used for sprains, muscular pain and inflamed joints. It is also applied in poultices to relieve pain and inflammation (Kohli et al., 2005).

**Ayurvedic uses:** In Ayurveda, rhizomes of *C. longa* are used for Visavikara, Kustha, Vrana, Tvagroga, Prameha, Pandu, Sitapitta, Pinasa, etc. (Anonymous, 1990). It is one of the ingredients of kashayas in Ayurveda; Manjishtaadi, which is used as a therapy for arthritis and skin diseases (Subramoniam et al., 2013).

**Pharmacological activities:** Different fractions of the petroleum ether extract of *C. longa* reported to have anti-inflammatory activity in cotton pellet induced inflammation in rat method (Arora et al., 1971). Oral administration of *C. longa* found to significantly reduce inflammatory swelling in rats with Freund’s adjuvant-induced arthritis (Arora et al., 1971). Anti-inflammatory activity of curcumin has been demonstrated in rats with Freud’s adjuvant-induced arthritis (Srimal et al., 1971; Srimal and Dhawan, 1973). Water soluble extract of *C. longa* and its curcumin component found to possess strong antioxidant activity (Toda et al., 1985). *C. longa* has also been found to have hepatoprotective activity against different hepatotoxic insults like galactosamine (Kiso et al., 1983), acetaminophen (Donatus et al., 1990), *Aspergillus* aflatoxin (Soni et al., 1992) and carbon tetrachloride (CCl<sub>4</sub>) in animal experiments (Deshpande et al., 1998; Park et al., 2000).

**Phytochemical studies:** Curcumin, a major active principle from *C. longa* is known to have multiple pharmacological properties such as anti-inflammatory, antiarthritic (Arora et al., 1971; Deodar et al., 1980; Shah et al. 2006), antifungal (Apisariyakul et al., 1995), antiviral (Bourne et al., 1999), antitumor (Kawamori et al., 1999), antibacterial (Negi et al., 1999), hepatoprotective (Park et al., 2000) and antispasmodic (Itthipanichpong et al., 2003). Curcumin was also found to be a very potent antioxidant (Sharma, 1976; Unnikrishnan and Rao, 1995; Osawa et al., 1995; Iqbal et al., 2003). Curcumin is one of the potential therapeutic agents in inflammatory bowel disease, arthritis, pancreatitis, chronic anterior uveitis, cancer, neurodegenerative diseases, cardiovascular diseases, allergy, asthma, bronchitis,
chronic kidney disease, diabetes, obesity, scleroderma and psoriasis (Jurenka, 2009; He et al., 2015). It is used as a chemopreventive and chemotherapeutic agent in diseases such as arthritis, cancer, diabetes and obesity (Zhou et al., 2011; Subramoniam et al., 2013). Curcuminoids isolated from *C. longa* have shown to possess anti-inflammatory activity in carrageenan induced rat paw edema model (Patil et al., 2011). Along with three curcuminoids (curcumin, demethoxycurcumin and bisdemethoxycurcumin) *C. longa* also contains volatile oils (natlantone, tumerone and zingiberone), proteins, sugars and resins. They are involved in controlling inflammation, cell growth and apoptosis (Gupta et al., 2012).

### 3.3.3 *Pongamia pinnata* (L.) Pierre

**Ethnobotanical uses:** The fresh bark of *P. pinnata* is used internally in bleeding piles, beriberi (Satyavati et al., 1987; Khare, 2004b), diabetes (Aiman, 1970) and as an antimicrobial (Koysomboon et al., 2006). Stem bark of *P. pinnata* is therapeutically used as an antiseptic in skin diseases and for its wound healing properties (Kurkure and Grampurohit, 2001). The plant is used for anti-inflammatory (Srinivasan et al., 2001), anti-plasmodial, anti-nociceptive, anti-hyperglycaemics, anti-lipidoxidative, antidiarrhoeal, anti-ulcer, anti-hyperammonic and CNS depressant activity (Li et al., 2006).

**Ayurvedic uses:** In Ayurveda, *P. pinnata* stem bark is used for Kustha, Kandu, Dustavrama, Prameha, Yoniroga, Krmiroga, Antrarvidradhi, Vidradhi (Anonymous, 1990).

**Pharmacological activities:** The anti-inflammatory activity of aqueous extract of *Pongamia pinnata* stem bark was evaluated in acute and chronic models of inflammation in albino rats, wherein significant anti-inflammatory activity without ulcerogenic activity was observed (Smitha et al., 2010). Badole et al (2012) evaluated the analgesic (acetic acid-induced abdominal writhing and hot plate test in mice) and anti-inflammatory (carrageenan and cotton pellet granuloma tests in rats) activity of alcoholic extract of stem bark. Ethanolic extract of stem bark has been studied for its anti-inflammatory potential in carrageenan induced paw edema and cotton pellet granuloma models and its analgesic activity was also analysed by acetic acid-induced writhing response in albino mice and tail flick method in albino rats (Sagar and Upadhyaya, 2013). In a study carried out by Prithima and Jayanthi (2015), aqueous extract of stem bark of *P. pinnata* was found to possess anti-inflammatory activity in
carrageenan-induced rat paw edema and analgesic activity in acetic acid-induced writhing response in albino mice and tail flick method in albino rats.

**Phytochemical studies:** The stem bark of the *P. pinnata* consist of several flavone and chalcone derivatives such as Pongone, Galbone, Pongalabol, Pongagallone A and B (Yadav et al., 2011).

### 3.3.4 *Terminalia chebula* Retz.

**Ethnobotanical uses:** Fruits of *T. chebula* are used to treat diabetes, colic pain, chronic cough, sore throat, asthma and digestive problems (Reddy et al., 2009).

**Ayurvedic uses:** In Ayurveda, fruits of *T. chebula* have various therapeutic uses like Vibandha, Aruci, Udavarta, Gulma, Udararoga, Arsa, Pandu, Sotha, Jirnajvara, Visamajvara, Frameha, Sirogoa, Kasa, Tamakasvasa, Hdroga (Anonymous, 1990). It is one of the ingredients of kashayas in Ayurveda; Mohaamanjishtaadi, which is used as a therapy for arthritis, rheumatoid arthritis, chronic skin diseases, anaemia, paralytic conditions, filariasis, ophthalmic diseases and obesity (Subramoniam et al., 2013).

**Pharmacological activities:** Various extracts and pure compounds from fruits of *T. chebula* have exhibited anti-oxidant activity (Cheng et al., 2003). Aqueous extract of fruits showed strong hepatoprotective activity (Lee et al., 2005, 2006). Ethanolic extract of fruits have also shown strong antioxidant activity against isoproterenol-induced oxidative stress in rats (Suchalatha et al., 2005). The fruit extract has also shown strong antibacterial activity against intestinal bacteria, *Clostridium perfingens* and *Escherichia coli* (Kim et al., 2006). Aqueous extract of the *T. chebula* showed lipid peroxidation and antioxidant activities on rat testis (Krishnamoorthy et al., 2007). Methanolic extract of *T. chebula* fruits have also shown anti-ulcer activity in experimental rats (Raju et al., 2009). The anti-arthritic effect of *T. chebula* hydroalcoholic extract was evaluated in either formaldehyde or complete Freund's adjuvant induced arthritis in rats (Nair et al., 2010). Study shows that acetone extract of *T. chebula* fruits have antiarthritic activity in CFA induced arthritis in rats (Ramani and Pradhan, 2012). Ethanolic extract of *T. chebula* fruits has proven its analgesic and anti-inflammatory activities using hot plate method and carrageenan induced paw edema model (Jami et al., 2014).

**Phytochemical studies:** *T. chebula* contains several phytoconstituents like tannins, flavonoids, sterols, amino acids, fructose, resin and fixed oils. There are about 14
hydrolysable tannins (gallic acid, chebulic acid, punicalagin, chebulanin, corilagin, neochebulinic acid, ellagic acid, chebulegic acid, chebulinic acid, 1,2,3,4,6-penta-O-galloyl-b-Dglucose, casuarinin, 3,4,6-tri-O-galloyl-D-glucose and terchebulin) which have been isolated from its fruits (Juang et al., 2004; Gupta, 2012).

3.4 **Dashamoola as a formulation**

Although, individual plants of *Dashamoola* have been studied for different activities, there are several reports where *Dashamoola* has been used as a formulation as mentioned below.

A clinical study has been conducted to study the role of *Brihat Dashamoola, Taila Nasya* and *Laghu Sutashekhara Rasa* in the management of *Ardhavabhedaka* with respect to migraine.

The patients receiving *Brihat Dashamoola Taila* along with *Laghu Sutashekhara* (52.94%) as compared to receiving *Laghu Sutashekhara Rasa* alone (35%) showed marked improvement indicating that combined treatment showed enhanced effect (Parekh and Rajagopala, 2009). A comparative clinical study of *Dashamoola Taila Matra Basti* and *Tila Taila Matra Basti* in *Kashtartava* (dysmenorrhea) was conducted. The dose was 60 ml per day for 7 days each cycle for two consecutive cycles. Significant and almost equivalent improvement was seen in symptoms in both groups (Karunagoda et al., 2010).

Decoction of *Dashamoola* was investigated for its anti-inflammatory effects in comparison with Diclofenac in animal models viz. carrageenan induced rat hind paw edema and cotton pellet implantation methods, wherein *Dashamoola* was found to be effective in comparison with Diclofenac sodium (Singh et al., 2011). Nephro, hepato and gastro toxic potential of aqueous extract of *Dashamoola* in comparison with Diclofenac sodium was evaluated in rat model and it was found that ulcer index of *Dashamoola* and Control group was significantly lower than the Diclofenac group, indicating that *Dashamoola* is significantly less toxic than the Diclofenac sodium (Dawane et al., 2012b).

*Dashamoola* kwatha has been studied for the management of stress induced chronic insomnia using shirodhara method. *Dashamoola* kwatha Shirodhara, half an hour daily in morning for the duration of 21 days showed significant relief on sleeplessness, distress, sleep time, sleep quality and freshness after awakening. Relief in mental health has been observed based on Hamilton’s Anxiety Rating Scale,
Hamilton’s Depression Raring Scale, Brief Psychiatric Rating Scale and Manasabhav pariksha on Ayurvedic parameters (Singh et al., 2013).

Efficacy of Dashamoolarishtha has also been evaluated in clinical study for perimenopausal cervicitis. After 90 days of treatment, statistically significant decrease in cervical redness, swelling and low backache was observed. Along with it, significant inflammatory changes in Pap smear test were also observed (Mohite et al., 2014).

A case study report has showed that Yogabasti by Dashmoolakwatha and Tila oil has role in the management of infertility caused due to Poly Cystic Overy Syndrome (PCOS). After 3 cycles of Yogbasti, patient had regular menses (regular ovulation) and after taking treatment for 3 months, patient was able to conceive (Thorwe and Choudhari, 2014).

Analgesic activity of Dashamoolarishta formulation was evaluated by using experimental models of pain viz. Hot plate model in mice, Tail clip model in mice and Tail immersion model in rats (Bhalerao et al., 2015).

Analgesic, anti-inflammatory and anti-platelet potential of Dashamoola in the form of arishta and kwatha was evaluated in rats using carrageenan-induced inflammation, protein content in model of peritonitis and granuloma weight in cotton pellet granuloma. Analgesic effect was evaluated by counting number of writhes in writhing model. Dashamoola formulation alone and its combination with aspirin showed comparable anti-inflammatory, analgesic and anti-platelet effects to aspirin (Parekar et al., 2015).

A clinical trial of Dashamoola ksheera basti in dysmenorrhea was conducted on 30 patients with 15 patients each in Group A - Dashamoola ksheera basti with chandraprabhavati and Group B – Chandraprabhavati alone. Group receiving combination has shown better results in reducing arthava kalaja shoola (Rachana, 2015).

3.5 Epidemiology of cervicitis

Previous studies have shown that women with M. genitalium infection have high risk (1.7-6.4 folds) of mucopurulent cervicitis (Manhart et al., 2003).

The prevalence of Chlamydia trachomatis, Neisseria gonorrhoeae, Trichomonas vaginalis and Mycoplasma genitalium, in women with sexually transmitted disease (STD), and the frequency of coinfections and relationship of each
organism to cervicitis were investigated. It was found that the prevalence of *M. genitalium* was highest among selected infectious organisms (Schlicht et al., 2004; Gaydos et al., 2009).

In sexually transmitted diseases *M. genitalium* infection is common and found to be associated with cervicitis. A high prevalence of infected sexual partners are indicative of a cause of sexually transmitted infection (Falk et al., 2005).

An observational study on prevalence and predictors of cervicitis in female sex workers in Peru was carried out. Cervicitis was found to be common in female sex workers and was predominantly nongonococcal and nonchlamydial in etiology (Pollett et al., 2013).

Although there is ample literature available for understanding of cervicitis and its pathogenesis still it is difficult to interpret the findings as universal. The motives may include the different causative factors and related pathology of the condition (Marrazzo and Martin, 2007). Considering the increasing incidences at Bharati Ayurveda Hospital, Pune, India, before going for clinical validation of formulation, it is of utmost importance to find out prevalence of cervicitis from area where patients belongs. Such study will also help to find out the required potential of newly developed formulation. The exact prevalence of cervicitis can be estimated from population-based data but it appears to be a common finding that is seen in a wide variety of clinical settings (Marrazzo and Martin, 2007).

### 3.6 Summary of review of literature

Despite the wide traditional use of roots of plants used in *Dashamoola*, especially in *Ayurveda* as well as ethnobotany, there are very few reports with respect to its pharmacological studies in the literature on the anti-inflammatory activity. Although, few efforts have been taken for anti-inflammatory potential of *Dashamoola* plants and *Dashamoola* formulations, by far the comparative anti-inflammatory potential of roots of 10 plants of *Dashamoola* and their combination has not yet been investigated.

Therefore, the present study was designed to investigate and clarify comparative anti-inflammatory potential of *Dashamoola* plants and their new combination formulation using animal models of inflammation to rationalize their therapeutic use; also a well planed survey to understand prevalence of cervicitis in particular populations before the clinical validation of new formulation.