Chapter 12 Summary and Conclusion
The decline of fertility and mortality has added 20 years to the average life span. By the year 2030 the proportion of those over 60 will be one person in three. Osteo-Arthritis is the most common of rheumatic diseases. It is the principal source of pain and disability in the elderly and the overall disease prevalence increases with age. The present study was an attempt to develop a transdermal drug delivery system for Diclofenac diethylammonium or Ketorolac tromethamine for alleviation of pain and for the treatment of arthritis. The main interest in such a dosage form resulted from its ability to prolong the release at the site of inflammation. Following conclusions can be drawn from the results obtained.

A transdermal drug delivery system containing the anti-inflammatory analgesic diclofenac diethyl ammonium acrylate pressure sensitive adhesive system was developed satisfactorily, for percutaneous absorption for prolonged relief (for at least 24 hours) from pain. The TDDS was found to be stable at accelerated stability conditions (40°C/75% relative humidity for a period up to six months. Based on this, a shelf life of twenty-four months was proposed for the formulation.

To optimize the penetration, and hence the absorption of drug from the transdermal patches, various penetration enhancers of the natural origin were tried. They included the terpene enhancers viz. Mentha oil, Lemon oil, eucalyptus oil, thymol, geraniol, and chamomile oil. Chamomile oil showed the maximum enhancement, (Enhancement ratio of 19.78) which is more than that of the reported for the best terpene enhancer, Geraniol, for Diclofenac sodium (Enhancement ratio 18.97).

Chamomile oil itself is used in traditional medicine as anti-inflammatory, analgesic, antispasmodic, bactericidal, febrifuge, wound healing and for headache and migraine, dermatitis and sensitive skin. Therefore, it can be considered to be safe with respect to any systemic or local effects due to the enhancer. TDDS did not show any signs of erythema, or necrosis and hence unlike the enhancers of synthetic origin chamomile oil showed no potential for skin irritation.
The elimination half-life of Diclofenac diethylammonium is prolonged from two hours (conventional tablet) to ten hours in human volunteers; hence the drug administered in the transdermal dosage form remains in the body for a longer period and thus exerts a sustained action.

In contrast to conventional formulations (cream, gels, ointments, etc) the transdermal drug delivery system provides a constant and continuous presence of the drug in the system at the site of action. Since the drug not only permeates and reaches the systemic circulation, but also concentrates itself at the site of action; thus making it possible to achieve maximum pharmacological effects and minimum side effects.

Avoidance of GI tract should mitigate the common direct toxicities of acute mucosal lesions, nausea, vomiting, and dyspepsia, diarrhea acute mucosal lesions, which occur secondary to high local concentrations of NSAID in the alimentary tract. The arthritic patients for whom these drugs are finally intended for, may be predisposed to gastrointestinal side effects because the disease causes the development of frail gastrointestinal mucosa with a decreased capacity to synthesize mucus, energy yielding molecules (adenosine triphosphate) and cytoprotective prostaglandin’s. It reduces drug detoxification capacity and production of drug carrier proteins (albumin).

Thus the formulation achieves its objective of providing relief from pain in the arthritic patients, which is generally the elderly population already suffering from gastrointestinal and renal problems. The formulation also provides for termination of medication if required at any time, this is particularly relevant for elderly patients who should be kept under strict medical control which is otherwise impossible to perform since they frequently consume diuretics or other co-medication. Hence, the dose calculation may not be possible for them. The transdermal drug product designed is more effective therapeutically in lesser dose as compared to conventional therapy. It targets the effected tissue directly and posses a longer duration of action. All these desirable characteristics of this formulation make it significantly better than the currently available dosage forms.