Abstract
1.0 Abstract

Cancer is a broad term for a large group of diseases that can affect any part of the body. Other terms used are malignant tumours and neoplasms. One defining feature of cancer is the rapid creation of abnormal cells that grow beyond their usual boundaries, and which can then invade adjoining parts of the body and spread to other organs. Treatment aims to cure, prolong life and improve quality of life for patients. Some of the most common cancer types, such as breast cancer, cervical cancer and colorectal cancer, have high cure rates when detected early and treated according to best practice. Principal treatment methods are surgery, radiotherapy and chemotherapy. The main objectives of chemotherapy are to prolong the life expectancy, improve quality of life and to prevent progression and metastasis of cancer. Herbal medicines are being embraced as an alternative solution to conventional chemotherapy which has severe side effects. Many herbs have been evaluated in clinical studies and are currently being investigated phytochemically to understand their anti tumor actions against various cancers. Ayurvedic therapy was found to be able to cure these chronic diseases better, which were previously not amenable to treatment by western medical practices, some of the herbal drugs have been scientifically proven to possess anticancer activity. Interest in polyphenols, and especially in curcumin as a chemotherapeutic and chemoprotective agent, has dramatically increased in recent years. Curcumin, the most explored of the curcuminoids, has received increasing interest in recent years. Curcumin has tremendous potential for the treatment or prevention of cancer and various other diseases like Rheumatoid arthritis, Multiple sclerosis, Alzheimer, cataract formation, pulmonary toxicity and fibrosis. Curcumin posses a favorable safety profile, supported by hundreds if not thousands of years of use by humans as a spice and in traditional medicines, despite of the diverse activities. Unfortunately Curcumin suffers from poor biopharmaceutical properties such as, low solubility, poor permeability, metabolism in enterocytes and extensive first pass metabolism. This limits its oral bioavailability and hinders its successful application to the treatment and prevention of these pathologies, as therapeutic concentrations are difficult to achieve at the site of action. By a systematic application of modern formulation approaches these biopharmaceutical barriers can be successfully overcome and the true potential of Curcumin can be fully exploited to alleviate and prevent the suffering due to these and
possibly other diseases. Such an industrially scalable formulation with enhanced bioavailability of curcumin has been developed, characterized and reported in this work. A self-nano-emulsifying drug delivery system (SNEDDS) was developed to improve solubility and subsequently oral bioavailability of curcumin. As part of this development, a HPLC method for the analysis of curcuminoids has been validated and has been used for the analysis of curcumin in various in vitro samples like solubility studies, dissolution studies and stability studies. A simple, specific and sensitive; LC/MS/MS based bioanalytical method has been developed and validated for the analysis of curcumin in plasma samples. The limit of quantification of this method has been established at 10 ng/ml. As part of pre formulation studies the intrinsic stability of curcumin has been studied and it has been shown to be stable against acid hydrolysis, extremely labile under base hydrolysis, labile under neutral hydrolysis, labile under oxidation and photolabile. The Solubility of curcumin has been studied in various oil and excipient and found to have low solubility in most with the exception of few like Transcutol and Cremophor. Curcumin has been shown to have a pH dependent solubility profile; being more soluble in alkaline pH than in acidic pH. Excipient compatibility studies have been carried out for curcumin with various excipients and it was found to be compatible with excipients used in the final formulation – Transcutol HP, Capryol 90, PEG 200 and Cremophor EL. A stable and industrially scalable Self Nano Emulsifying Drug Delivery System (SNEDDS) formulation has been developed for curcumin using established excipients within reported levels. The SNEDDS formulation has been shown to give rapid, reproducible, complete and pH independent release of curcumin producing a nanoemulsion with particle size in the range of 90 nm. The SNEDDS formulation has been shown to have a significantly higher bioavailability in rats in comparison to curcumin suspension showing a 4 times increase in AUC and 8 times increase in Cmax at the same dose level. MTT assay on human lung cancer lines further ascertained the efficacy of curcumin against lung cancer and it was found that IC 50 value of curcumin SNEDDS was nearly half of what we obtained from curcumin. This indicated that SNEDDS helped in enhancing the efficacy of curcumin against lung cancer and holds great potential in its treatment.