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Biodegradable injectable in situ depot-forming PLGA for controlled release of paclitaxel

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Development of new drug molecule is expensive and time consuming. Improving safety efficacy ratio of "old" drugs has been attempted using different methods such as individualizing drug therapy, dose titration, and therapeutic drug monitoring. Delivering drug at controlled rate, slow delivery, targeted delivery are other very attractive methods and have been pursued vigorously. It is interesting to note that considerable work and many publications from USA, Europe are authored by Indian researchers.[1–3] Numerous animal and human investigations have provided an increased understanding of the pharmacokinetic and pharmacodynamic principles that govern the action and disposition of potent opioid analgesics, inhalation anesthetic agents, sedative/hypnotics, and muscle relaxants. These studies suggest that skin and buccal and nasal mucous membranes may have use as alternate routes of analgesic and anesthetic delivery. Similar developments with other compounds have produced a plethora of new devices, concepts, and techniques that have together been termed controlled-release technology (CRT). Some examples of CRTs are transdermal and transmucosal controlled-release delivery systems, ml6 nasal and buccal aerosol sprays, drug-impregnated lozenges, encapsulated cells, oral soft gels, iontophoretic devices to administer drugs through skin, and a variety of programmable, implanted drug-delivery devices. There are a number of factors stimulating interest in the development of these new devices, concepts, and techniques. Conventional drug administration methods, while widely utilized, have many problems that may be potentially overcome by these methods. Equally important, these advances may appear attractive relative to the costs of new drug development. Rising research and development costs, alternative investment opportunities for drug firms, fewer firms conducting pharmaceutical research, and erosion of effective patent life have resulted in a decline in the introduction of new chemical entities since the late 1950s. Bringing a new drug through discovery, clinical testing, development, and regulatory approval is currently estimated to take a decade and cost well over $ 120 million. Novel drug delivery systems may account for as much as 40% of US marketed drug products by 2000. The purpose of this study is to develop Cremophor® EL-free in situ depot forming loaded with paclitaxel (PTX), able to improve the therapeutic index of the drug and devoid of the adverse effects of Cremophor® EL.

Injectable in situ-forming implant have received considerable attention as localized drug delivery systems. Here, we examined a poly-(DL-lactic-co- glycolic) acid (PLGA) as an injectable drug depot for paclitaxel (Ptx). In vitro experiments showed that Ptx was released from PLGA over the course of more than 30 days. The release profile shows a slow diffusion-controlled phase, followed by a more rapid degradation-controlled region. Two semi-empirical mathematical models (Power law and Peppas) were applied to drug release data in order to elucidate release mechanisms and kinetics. In order to confirm the results of drug profile release, study of the polymer degradation process for the direct determination of the monomer(s): lactic acid (LA) and glycolic acid (GA) with a new HPLC method is proposed. Generally, High-performance liquid chromatography or high-pressure liquid chromatography (HPLC) is a chromatographic method that is used to separate a mixture of compounds in analytical chemistry and biochemistry so as to identify, quantify or purify the individual components of the mixture. Reversed-phase HPLC or Ultra-high Performance Liquid Chromatography (UHPLC) is a commonly used separation mode. It provides dynamic retention of compounds possessing hydrophobic and organic functionality. A combination of hydrophobic and van der Waals type interactions between all the target compound and both the stationary and mobile phases enables the retention of these compounds by reversed phase. In very small amounts, the sample mixture to be separated and tested is sent into a stream of mobile phase percolating via a column. There are different types of columns available with sorbents of varying particle sizes and surfaces. The mixture moves through the column at varying velocities and interacts with the sorbent, also known as the stationary phase. The velocity of each component in the mixture depends on 1) its chemical nature, 2) the nature of the column and 3) the composition of the mobile phase. The time at which a specific analyte emerges from the column is termed as its retention time. The retention time is measured under specific conditions and considered as the identifying characteristic of a given analyte. Sorbent particles might be hydrophobic or polar in nature. The commonly used mobile phases include any miscible combination of water and organic solvents such as acetonitrile and methanol. Water-free mobile phases can also be used. The aqueous component of the mobile phase might

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contain acids like formic, phosphoric or trifluoroacetic acid or salts to enable the separation of the sample components. The composition of the mobile phase is either maintained as a constant or as varied during the chromatographic analysis. The constant approach is effective for the separation of the sample components that are not very dissimilar in their affinity for the stationary phase. In the varied approach, the composition of the mobile phase differs from low to high eluting strength. The eluting strength of the mobile phase is reflected by analyte retention times where high eluting strength produces fast elution.

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