بسم الله الرحمن الرحيم

شبكة المعلومـــــات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

﴿ قـــسـم ﴾

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
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15 – 25c and relative humidity 20-40 %

بعض الوثائق الأصلية تالفة

بالرسالة صفحات

لم ترد بالأصـــل

DEVELOPMENT AND IN-VITRO EVALUATION OF SOME COLON-SPECIFIC DRUG DELIVERY SYSTEMS

A Thesis presented by

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DEPARTMENT OF INDUSTRIAL PHARMACY
FACULTY OF PHARMACY
UNIVERSITY OF ALEXANDRIA

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DEDICATED

To

My parents, My Wife,

&

My Sister.

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1. Terminology of drug targeting

The idea of drug targeting to a specific site in the body was first introduced almost a century ago. In recent years this field has emerged as an important area of research. This long delay was attributed to the inadequate understanding of various diseases; the lack of a detailed description, at the cellular-molecular level, of how drugs are processed; and the difficulties in identifying and producing carrier molecules specific to the targeted organs, cells, or tissues. Most drug therapies currently available provide little, if any, target specificity [1].

A target-oriented drug delivery system must supply drug selectively to its site(s) of action(s) in a manner that provides maximum therapeutic activity through controlled and predetermined drug-release kinetics. It should prevent degradation or inactivation during transit to the target sites, and protect the body from adverse reactions because of inappropriate disposition. Requirements for target-oriented drug delivery also include that the delivery system should be biochemically inert, nonimmunogenic, and physically and chemically stable in vivo and in vitro. The carrier must be biodegradable, or readily eliminated without any problem; and the preparation of the delivery system must be reproducible, cost-effective and reasonably simple [1].

Drug targeting has been classified into three types:

A- First-order targeting: describes delivery to a discrete organ or tissue.

B- Second-order targeting: represents targeting to a specific cell type(s) within a tissue or organ (tumor cells).

C- Third order targeting: implies delivery to a specific intracellular compartment in the target cells (e.g., lysosomes cells).

Basically, there are three approaches for drug targeting. The first approach (magic bullet approach of Ehrlich) involves the use of biologically active agents that are both potent and selective to a particular site in the body. The second approach (prodrug approach) involves the preparation of pharmacologically inert forms of active drugs that when they reach the active sites become activated by a chemical or enzymatic reaction. The third approach (magic gun or missile approach) utilizes a biologically inert macromolecular carrier system that directs a drug to a specific site in the body where it is accumulated and affects its response.

Regardless of the approach, the therapeutic efficacy of targeted drug delivery systems depends on the timely availability of the drug in active form at the target site(s) and its intrinsic pharmacological activity. The intrinsic pharmacokinetic properties of the free drug should be the same, irrespective of whether or not it is introduced into the body attached to a carrier[2].

There are several factors that determine the availability of drug at the target site. These include the rates of input of targeted drug into the body plasma, distribution of targeted drug to the active site, release of active drug from the formulation at the site of action, removal (elimination) of targeted drug from the target site, diffusion or transport of targeted drug and free drug from the active site to nontarget sites, and blood and lymph flow to and from the target site[3].

2 . Targeted drug delivery systems

2.1 . Prodrugs

A prodrug is pharmacologically inert form of an active drug that must undergo transformation to the parent compound in vivo by either a chemical or an enzymatic reaction to exert its therapeutic effects. Prodrugs are designed to alter the absorption, distribution, and