

CHAPTER 10.

IV-VIII.
PARENTERAL,
NASAL,
OCULAR,
PULMONARY, &
VAGINAL
CONTROLLED RELEASE
DOSAGE
FORMS

CHAPTER 10.

IV. PARENTERAL CONTROLLED
RELEASE DOSAGE FORMS

1921

Insulin extract provides
hope for diabetics

In research using dogs, Canadian physicians Frederick Banting and Charles Best have managed to isolate the hormone insulin, which will help to treat people suffering from diabetes. Insulin is a hormone produced by the pancreas, which helps body cells to absorb energy-giving glucose. However, in people suffering from diabetes, the pancreas does not produce enough insulin, so that blood sugar levels rise alarmingly, often leading to death. Banting and Best artificially created diabetes in dogs by tying off their pancreatic ducts. They isolated insulin from cells produced by the pancreas and injected it into the dogs, which were cured.



▲ Frederick Banting, one of the scientists who has isolated the hormone insulin.

RX-PRODUCT NEWS: PIPELINE

A Direct Channel of Information

3Q 2004, March 2004

Peginterferon alfa-2b
PEG-INTRON

Pharmaceutical

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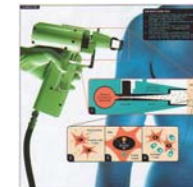
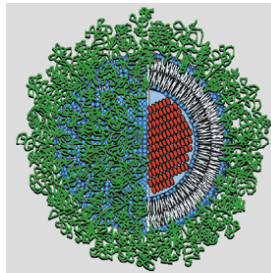
Pharmaceutical

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Take These Genes and
Call Me in the Morning

Gene therapy: A patient's cells are treated with DNA containing genes that...

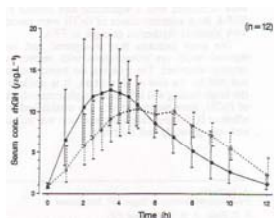


Fig. 1 Serum concentrations of rhGH (geometric mean with SD) after single dose subcutaneous administration of 5 IU rhGH by jet-injection (—●—) and needle-injection (—○—). Levels of rhGH were below the lower limit of quantitation (1.50 ug/L¹⁷) in all subjects at 16, 20 and 24 h after dosing.

DUPLEX Drug Delivery System

E. Braun Medical Inc. (Bethlehem, Pa.) recently introduced the DUPLEX Drug Delivery System. It is designed to simplify intravenous (IV) antibiotic delivery to patients, minimize the potential for medication errors, eliminate the pharmacy labor component of IV antibiotic delivery, and reduce drug waste. The DUPLEX system consists of a pre-filled bag containing proper doses of drug and diluent in different compartments separated by a quick-release seal. The bag is free of polyvinyl chloride, bis(2-ethylhexyl) phthalate, and latex. The caregiver simply swabbers the bag to mix the drug and diluent and prior to administration. The product can be stored at room temperature and does not require a messy thawing process. Special inorganic and moisture-barrier technologies are employed to protect the drug powder from water and oxygen transfer through the bag over the product's shelf life. The DUPLEX system is equipped with a Uniform Code Council (UCC) 649-128 bar code that references the final antibiotic. This bar code can be used to reduce medication errors, automate patient charting, track inventory, and facilitate reimbursement tracking. For more information, visit www.braunusa.com, or call 800-227-2862.

CHAPTER 10.

V. NASAL CONTROLLED
RELEASE DOSAGE FORMS

NOW AVAILABLE
The first needle-free flu vaccine in the U.S.

New
FluMist
Influenza Virus Vaccine
Live, Intranasal

Ask your health care professional if FluMist, the first needle-free flu vaccine, is right for you and your family.

FluMist is indicated for healthy children, adolescents, and adults 18 to 49 years of age. FluMist can help prevent the flu for the entire season.

In studies of approximately 2,000 people between the ages of 6 and 49, side effects were generally mild and temporary. FluMist was well tolerated. Other live-attenuated vaccines used for comparison, such as intranasal, single-use, single-dose, intranasal, live-attenuated, influenza, and trivalent, whole-virus, live-attenuated, intranasal, live-attenuated, influenza, were not used in studies as placebo when FluMist is used in a larger population. There are very rare reactions with all vaccines, including FluMist. FluMist does not protect 100% of individuals vaccinated. FluMist should not be used under any circumstances in anyone with an allergy to any part of the vaccine, including eggs or gelatin. It should not be used in anyone with a history of Guillain-Barre syndrome, and it should not be used in anyone with a history of severe asthma. FluMist should not be used in anyone with a history of severe asthma, asthma, or multiple allergic diseases should not get FluMist. See additional information on Precautions/Warnings.

For more information or to find a FluMist provider in your area, visit www.fluMist.com or call 1-877-FluMist.

Snuffing Out Flu

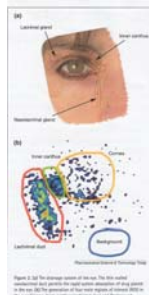
INFLUENZA kills 20,000 people a year in the United States alone. Vaccinations can prevent the spread of flu, but who likes shots? Now there's an alternative: a nasal spray administered by doctors or nurses. The spray vaccine is at least as effective as flu shots. In clinical trials this year, only 1 percent of the 1,070 children who received the spray got the flu. Invented at the University of Michigan School of Public Health, the vaccine spray could be available by prescription within two years. www.ajron.com

CHAPTER 10.

VI. OCULAR CONTROLLED RELEASE DOSAGE FORMS

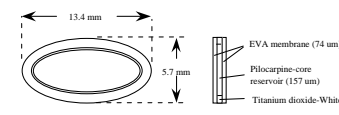
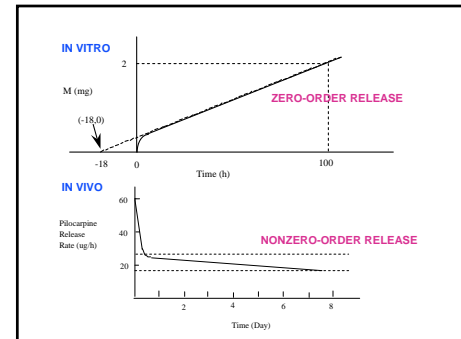
FACTORS AFFECTING INTRAOCULAR BIOAVAILABILITY

1. LIMITED ABILITY OF THE OCULAR CAVITY TO HOLD DRUG SOLUTION.
2. PRESENCE OF LACRIMAL FLUID.
3. NASOLACRIMAL DRAINAGE.
4. PROTEIN BINDING.
5. NONPRODUCTIVE ABSORPTION.


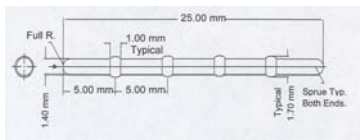
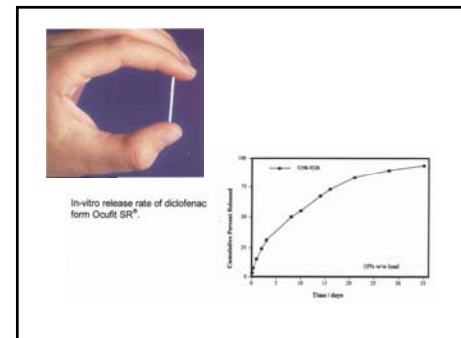
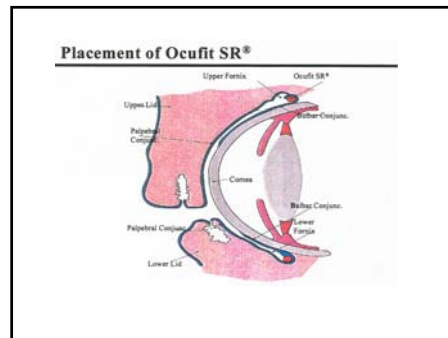


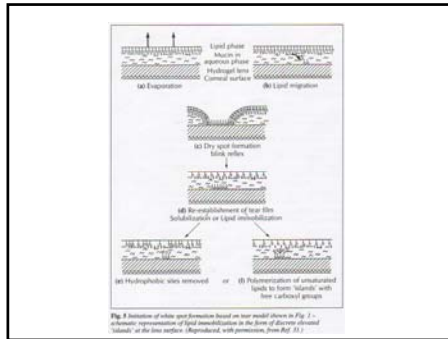
APPROACHES FOR IMPROVED OCULAR DELIVERY

1. USE OF DRUG SUSPENSION
2. USE OF VISCOSITY ENHANCING AGENT
3. OCUSERT SYSTEM
4. OCUFIT SR SYSTEM
5. DURASITE

OCUFIT SR SYSTEM

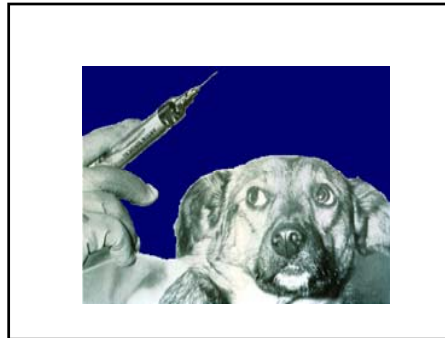


Xal-Ease
Pfizer Ophthalmics (New York, NY), a new business unit of Pfizer Inc, announced FDA approval for Xal-Ease, a handheld eyedrop delivery aid designed exclusively for Xalatan (latanoprost ophthalmic solution). Xalatan, a prescription eyedrop for the treatment of open-angle glaucoma and ocular hypertension, is the first and only drug in its class with a specialized delivery aid. The one-touch push button in the Xal-Ease system is designed to dispense a single drop into the eye every time. For more information, visit www.xalatan.com.

Xal-Ease
http://www.anatomyoftheeye.com/xalatan_users/xal-ease/

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CHAPTER 10.
VII. PULMONARY CONTROLLED RELEASE DOSAGE FORMS



Injection Alternative

LOCAL AND SYSTEMIC EFFECT DELIVERY OF PROTEIN DRUGS

BRANCHES OF THE BRONCHIOLES

SURFACE AREA OF THE AIRWAYS
SURFACE AREA OF THE ALVEOLI (TERMINAL 4 BRANCHES)

Epithelial Comparison

DRAMATIC DECREASE IN THE THICKNESS OF THE EPITHELIAL LAYER

The upper respiratory tract (the trachea and bronchial tree) is lined with a thick, folded, mucosa-covered wall. Most inhaled drugs available today are deposited here or in the mouth with traditional delivery methods where the major portion of each dose is retained in the throat and swallowed.

In adults, the alveolar tissue of the deep lung provides over 1,000 square feet of potential absorption surface area, lined with a very thin, highly permeable, non-ciliated, mucosa-free cell layer. The bubble system efficiently delivers compounds to this tissue for subsequent systemic absorption.

Current Aerosol Approaches



The Inhale
dry powder
delivery
device



UNIT DOSE BLISTER PACK



DRUG CLOUD IN THE HOLDING CHAMBER

Technical Challenges

- Efficient & reproducible deep-lung delivery.
- High yield 1-5 μm protein powder production
- Room temperature stable aerosol powders
- Fine powder micro-filling
- Easy-to-use portable system

PREVENTION OF PARTICLE AGGREGATION

Corrosion results in a carrier-drug bond strength sufficient for processing and also weak enough for effective delivery during inhalation.

PassCAL

CHAPTER 10.

VIII. VAGINAL & INTRAUTERINE CONTROLLED RELEASE DOSAGE FORMS

IN THE MOOD FOR LOVE

Some women hate having pills. Others cringe at the thought of implants or injections. Now there's a new choice for long-term birth control. In early October the FDA approved use of the **Mirena**, a thin flexible plastic ring that women can tuck like a rubber band and insert once a month into the vagina. Moisture and body heat activate the release of the same progestin and estrogen found in low-dose birth-control pills. Its makers say that Mirena is just as effective at preventing pregnancy and may cause fewer complications than the Pill.

◆ INVENTOR: Organon
◆ AVAILABILITY: May 2002
◆ TO LEARN MORE: find.mirena.com

HEALTH Rebirth of a contraceptive?

A cloud has hung over intrauterine devices ever since the Dalkon Shield was withdrawn in 1975 following reports of infections, miscarriages, and deaths. Last week the Food and Drug Administration approved a new version that might overcome the stigma. Most IUDs have not had safety problems, although they often work by irritating the uterine lining. The new device, Mirena, instead releases a trickle of a hormone often used in birth-control pills. Because the hormone is delivered right to the uterus, Mirena should have fewer side effects than the pill, say its developers from the Population Council in New York. And it remains effective for up to five years.

"Forget about what you think of IUDs," says Eloi Johannson, vice president of the Population Council, which licensed Mirena to Berlex Labs of Montville, N.J. He says the device has had a good safety record with more than 2 million women in Europe. It's not for women who have had ectopic pregnancies or pelvic inflammatory disease, however.

—Stacey Schultz

On the market again: It protects for as long as 24 hours and is safe and easy to use

Comeback of a Contraceptive
The sponge returns



Success is an elusive science. When Bruce "The Inventor" Carrigan who founded M22 first developed the sponge, it was a simple, one-time use device. Carrigan spent a year in the lab, but the product never made it to market. It was too expensive to produce, and the sponge was too bulky to carry. Carrigan spent a year in the lab, but the product never made it to market. It was too expensive to produce, and the sponge was too bulky to carry. Carrigan spent a year in the lab, but the product never made it to market. It was too expensive to produce, and the sponge was too bulky to carry.


APRIL 12, 1999 NEWSWEEK 69

HYCORE-V


Clinical Development

Cancer Pain
Core is completing a "Quality of Life" study which is taking place in hospices throughout the U.K. and France in support of a UK Marketing Authorisation with Approval expected in 1999. European wide applications will follow the "mutual recognition of national authorizations" route once approval is gained in the UK. In the USA, the first pivotal clinical trial will commence in 1999.

Post-operative Pain
Core is also extending the indications for Moraxan™ to include post-operative pain. A pilot efficacy study has been completed in the UK and, based on the results, will progress to a pivotal study which will commence early in 1999.



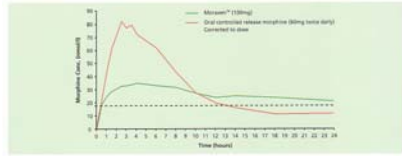
The unique non-biodegradable pessary has been developed to meet these criteria by incorporating metronidazole into the Moraxan™ delivery system with controlled drug release over a 24-hour period. The pessary is shown below at which is retained within an overcoat with a withdrawal string, is inserted and shaped of like a regular tampon. This pessary is already familiar to many women.



all Non-Operative and Hospital Hycore™
all Hycore™ in Application

Clinical Evaluation

The product is designed to release a constant level of morphine over 24 to 30 hours. Pivotal pharmacokinetic studies with Moraxan™, in volunteers, gave evidence of good absorption and sustained plasma levels of morphine, covering a minimum period of 24 hours while the suppository was in situ. The Hycore™ unit will continue to release morphine for up to 30 hours. The Hycore™ unit is expelled naturally or by stimulating a bowel movement whereupon it should be immediately replaced by another.



Morphine Blood Levels - Single Dose Crossover Study in 20 Subjects

The pill has company: the patch, the shot

Birth Controls

It's not just the pill that's changing the way women control their fertility. There are now three other options: a patch, a shot, and a ring. Each has its own advantages and disadvantages. The patch is a small, adhesive, rectangular piece that sticks to the body and releases hormones. The shot is a hormone injection that is given every three months. The ring is a flexible, ring-shaped device that is inserted into the vagina and releases hormones.



healthy woman

New: Permanent Birth Control

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AIDS A NEW SHIELD OFFERS NEW HOPE

The AIDS microbicide has always belonged to the same class of medical miracles as the cancer vaccine: ideal but elusive. Two years ago the top prospect was non-oxymol B, a topical gel for women that prevented transmission by killing HIV on contact. But it also killed healthy cells, giving viruses a point of entry in damaged tissue. Those who remember non-oxymol B may be skeptical about the latest contender: a seaweed-derived gel called Carra-guard. But it may bring real hope. Easy to use and compatible with condoms, the gel has no known side effects, blocks other STDs and allows women to conceive (a contraceptive version is on the way). Carra-guard doesn't work like non-oxymol B; rather than kill viruses, it binds to them so they can't enter the blood-

stream. But what's truly groundbreaking is its potential for poor, AIDS-ravaged regions like Africa. Odorous and undetectable, the gel could be a lifesaver for women whose partners refuse to use protection—as long as it's sold for pennies. The need to keep prices low has thus far deterred most pharmaceutical companies from pursuing microbicide research. Carra-guard's creator, the Population Council, is a tiny nonprofit funded by donors like the Gates Foundation, which has pledged \$20 million toward clinical trials starting in the fall. If those succeed, says Population Council researcher Janine van de Wijngaert, drugmakers may finally get involved by manufacturing the gel. She adds: "Let's hope they don't jack up the price."

MARY CARROLL



THE CELL: Big potential

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