Transdermal Drug in Adhesive Delivery Patch

A Technology Outline

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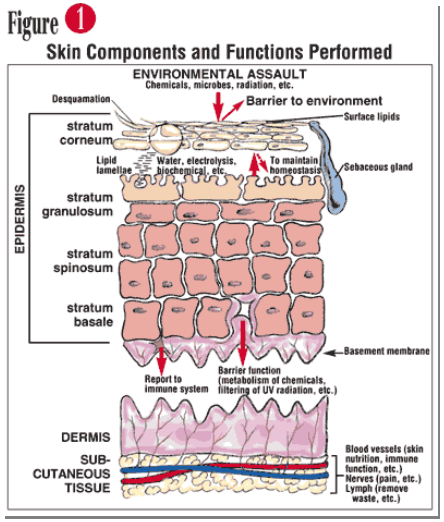
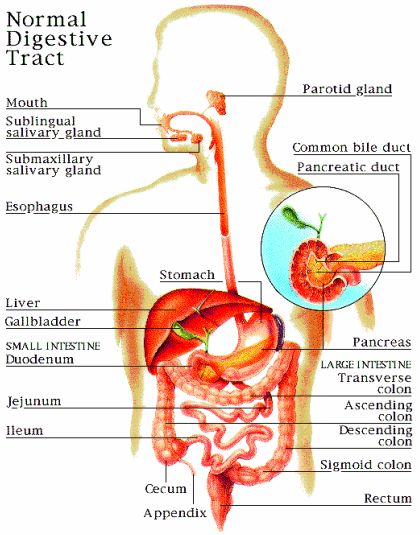
International Advanced Bio-Pharmaceutical Industries

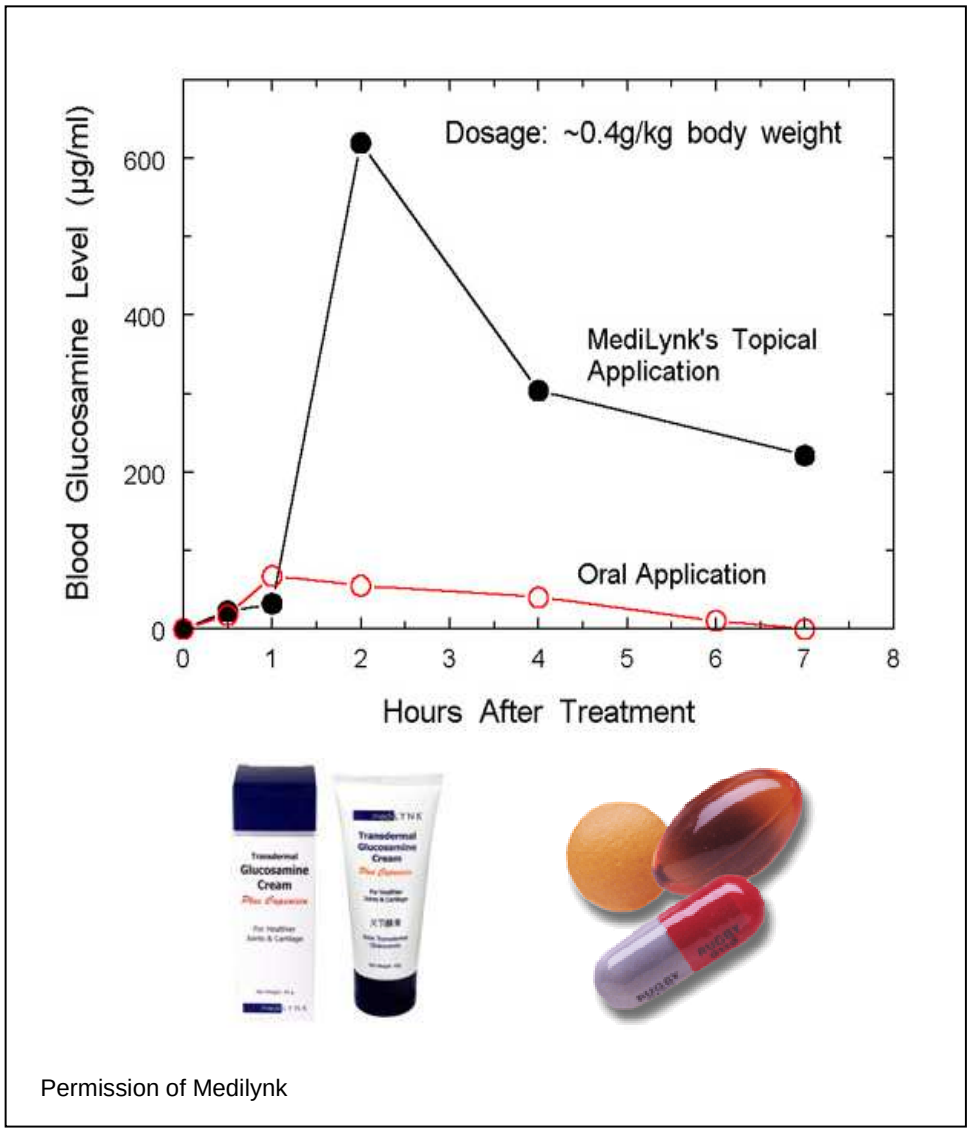
Transdermal Drug Delivery Offers the Best of IV and Oral Administration

	IV	Oral	TDD
Reduced liver first-pass effects	Yes	No	Yes
Constant drug levels	Yes	No	Yes
Self-administration	No	Yes	Yes
Unrestricted patient activity	No	Yes	Yes
Non-invasive	No	Yes	Yes





Transdermal Delivery is a more effective route



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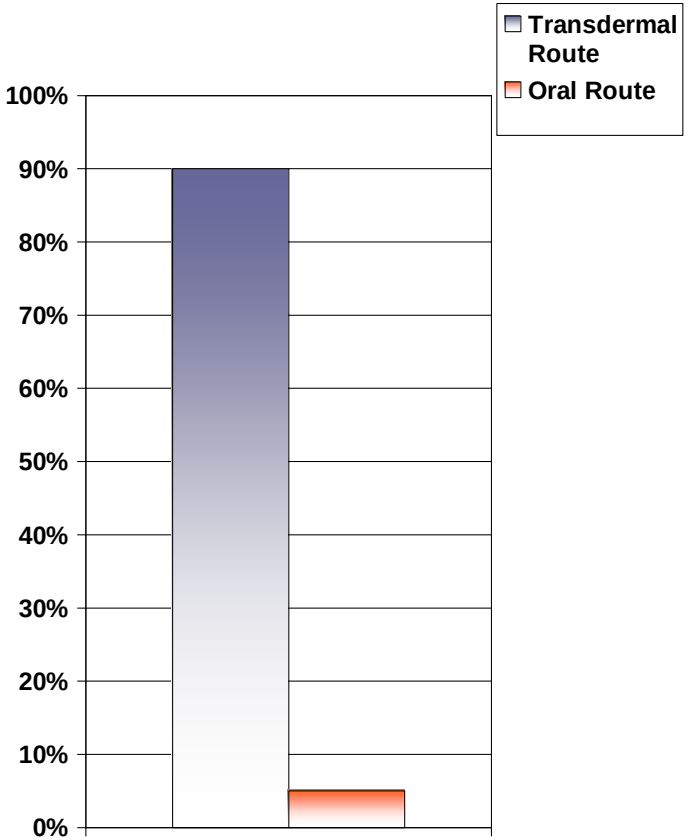


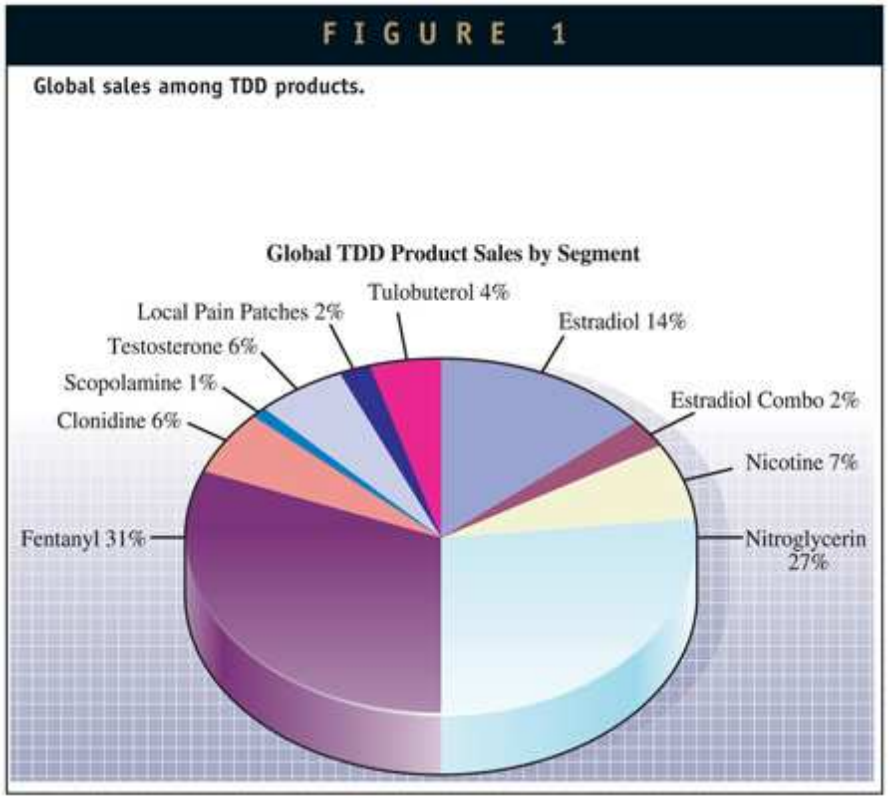
Commercialized TDDP products

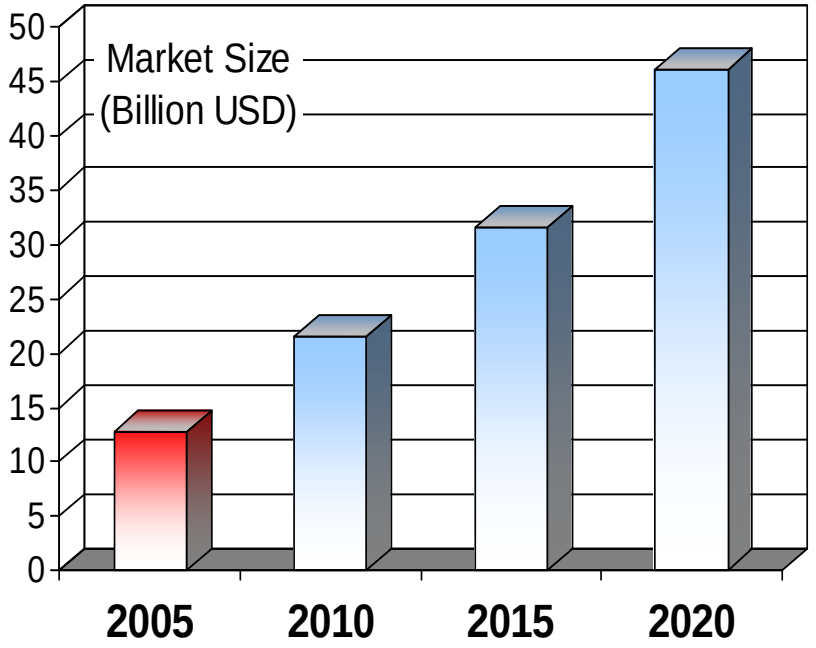
Table 1. Characteristics of Several Drugs Delivered Transdermally

Active Ingredient	Mol. Wt. (Daltons)	Trade Name(s)	Daily Dose	Frequency of Application	Type of System
Clonidine	230	Catapres-TTS®	0.1–0.3 mg	Weekly	Reservoir
Estradiol	272	Esclim® Vivelle® Vivelle-Dot® Climara®	0.025–0.1 mg	Weekly	Drug-in-adhesive
Ethinyl Estradiol w/ Norelgestromin	296 328	Ortho-Evra®	0.15 mg 0.02	Weekly	Drug-in-adhesive
Fentanyl	337	Duragesic Transdermal System®	0.6 mg	Once every three days	Reservoir
Lidocaine	234	Lidoderm®	Not stated	Daily	Drug-in-adhesive
Nicotine	162	Nicoderm CQ® Nicotrol®	7–21 mg	Daily	*
Nitroglycerine	227	Nitro-Dur® Nitrodisc®	1.4–11.2 mg	Daily	Drug-in-adhesive Reservoir
Scopolamine	303	Transderm-Scop®	0.33 mg	Once every three days	Reservoir
Testosterone	288	Androderm®	2.5–5 mg	Daily	Reservoir

* Because these are OTC products, the manufacturer is not required to describe the formulation.

Global TDD Market

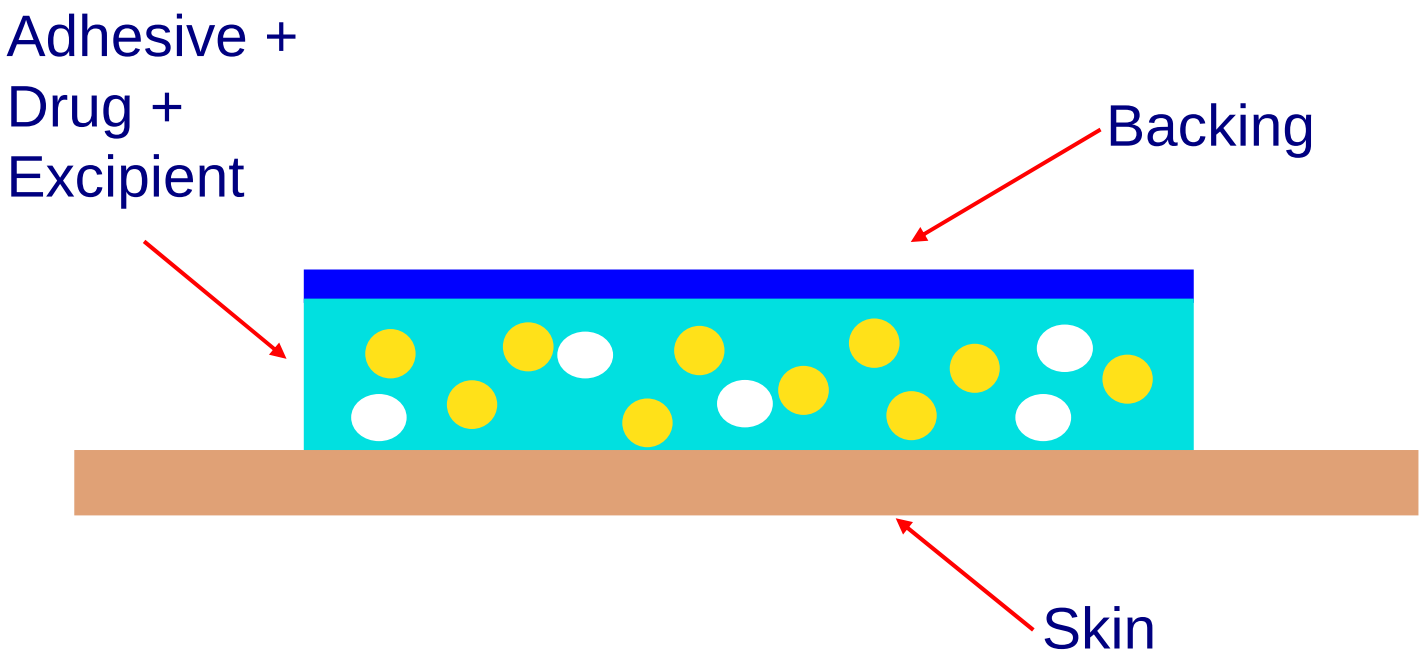




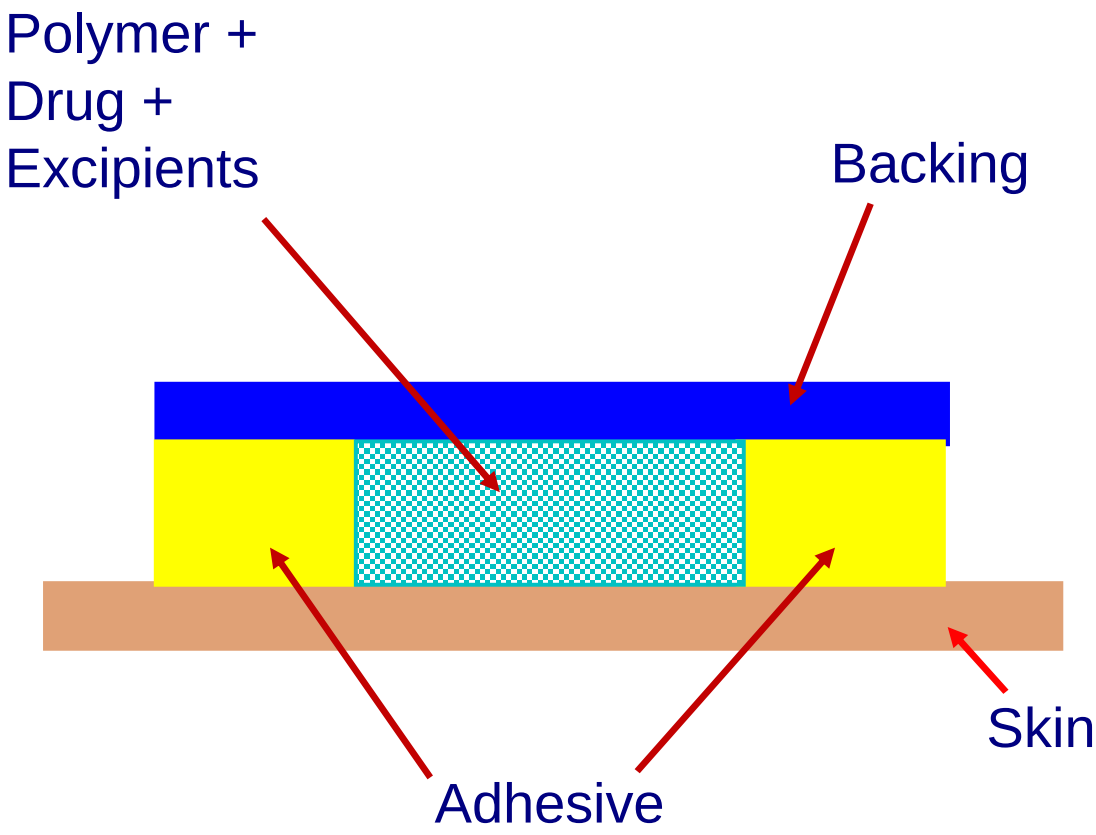
Source:

Jain Pharma Biotech Strategic Report (October 2006)

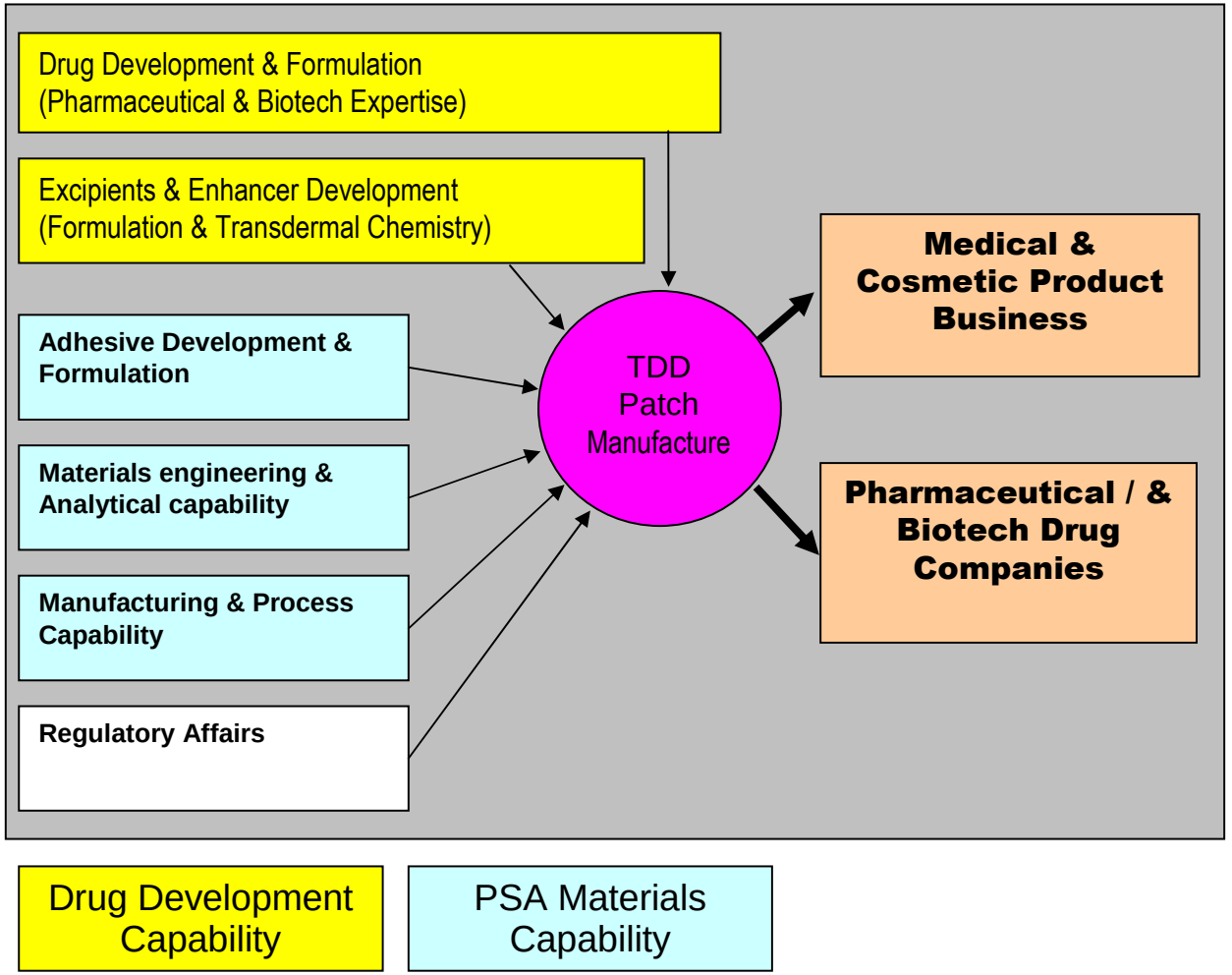
Design of a Transdermal Patch - Adhesive-Matrix Patch



Design of a Transdermal Patch - Polymer-Matrix Patch



Basic Building Blocks of TDDP Manufacturing



Typical Matrix Patch Manufacturing Process

Active Pharmaceutical Ingredients supply

Enhancer Encapsulation

Drug in Adhesive Compounding

Patch Manufacturing

Patch Converting

Patch Packaging

Typical TDDP
Product Development Cycle

FIGURE 1

Component selection for a transdermal drug delivery system must occur early in the development process.

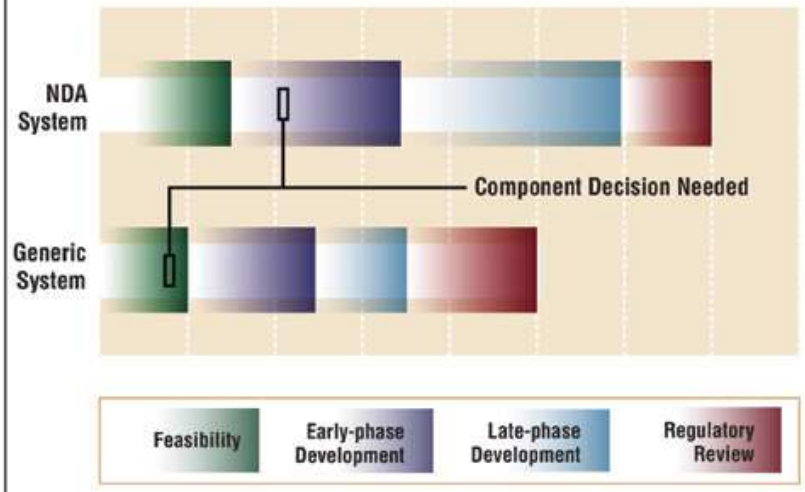
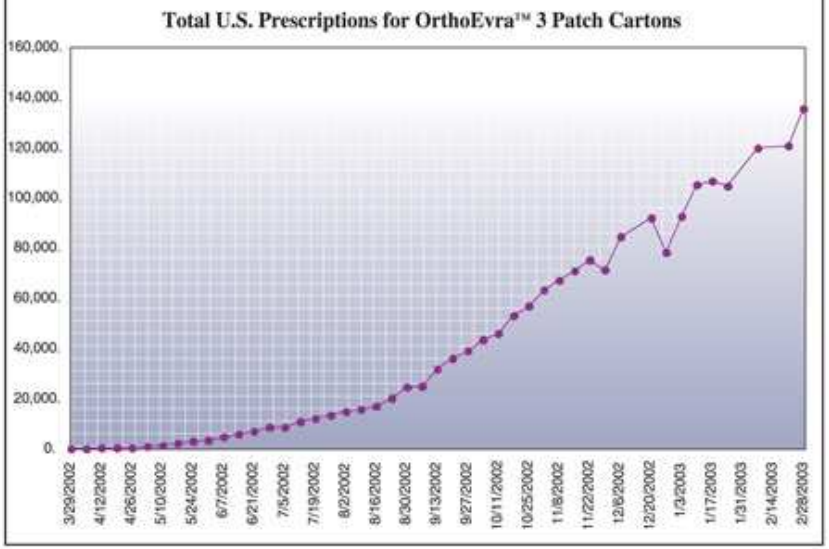


FIGURE 2

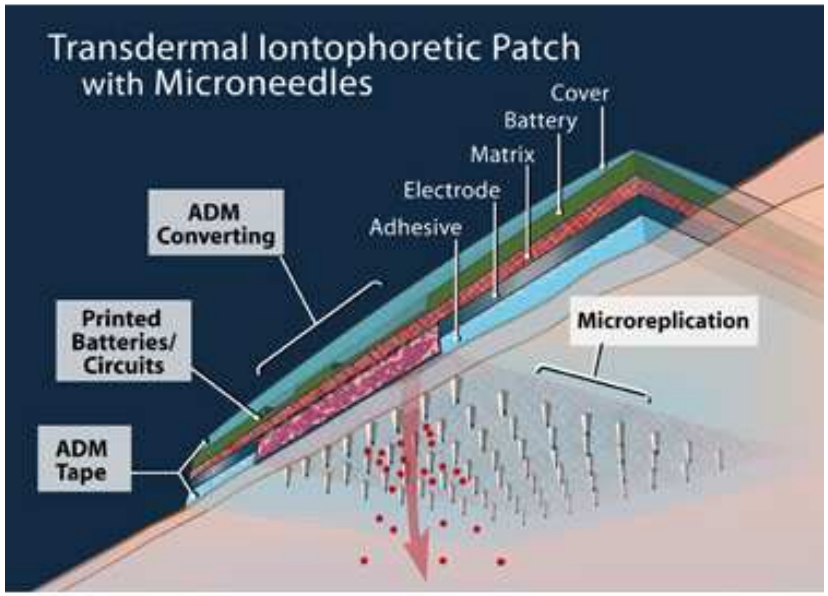
Total prescriptions of a 7-day contraceptive TDD product (OrthoEvra™) in the U.S



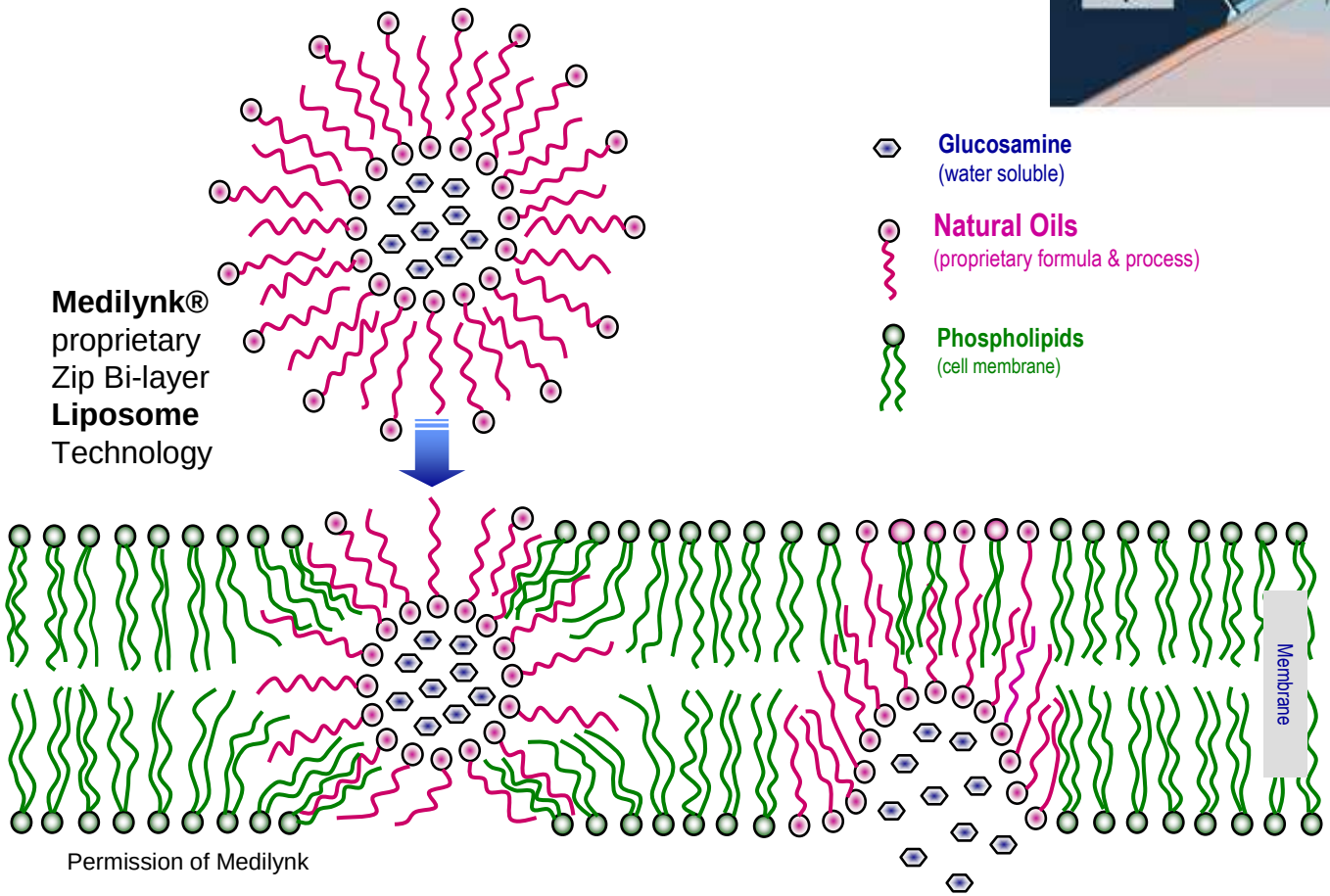
Transdermal Technologies

Transdermal Technology	Mode	Molecular Weight Dalton (g/mole)
Passive Diffusion	Passive	<500
Thermal	Active	<500
Chemical Permeation Enhanced	Passive	<500
Liposome / (Encapsulation)	Passive	???
Magnetophoresis / (Magnetic field)	Active	???
Iontophoresis / (Electrical charge)	Active	No Limits
Sonophoresis / (Ultra sound)	Active	No Limits
Microporation / (Micro needle)	Active	No Limits

Examples of Transdermal Enhancer Technologies



Medilynk® proprietary Zip Bi-layer **Liposome** Technology



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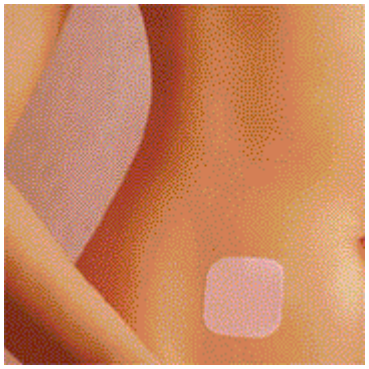
Current Scope of TDDP Therapeutic Application



- Hormone Replacement Therapy (HRT)
- Estrogen Replacement Therapy (ERT)
- Cardiovascular
- Oral Contraception
- Pain Management
- Asthma/Respiratory
- Smoking Cessation/Addiction Medication
- Urinary Incontinence/Gastro-Urinary
- Antiemetics
- Nutrition
- Cosmetics
- Sports Medicine
- Immunization

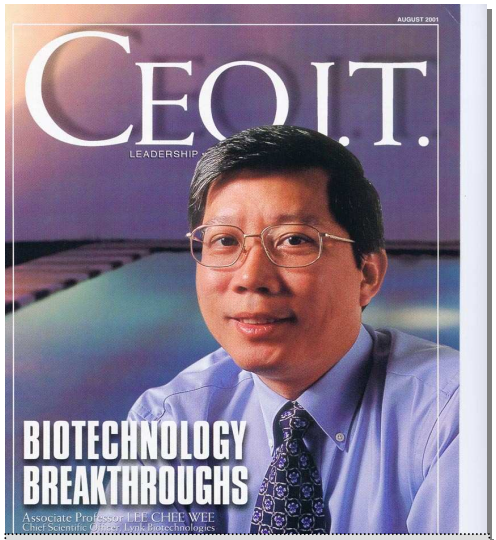
Strong Pharmaceutical Advisory & PSA Materials Engineering Support
to products solutions

Principal Consultant
LEE Chee Cheow
M.Sc., B.Sc.(Hons).

Chief Executive Officer
IABPI Pte. Ltd.
LEVERA Pte Ltd.

We provide:

- Pharmaceutical expertise in TDD formulation and clinical validation.
- Leading edge emulsion based transdermal drug delivery platform with continuous development & improvements.
- TDD Patch manufacturing is back up by solid PSA label materials manufacturing expertise.



Chief Scientific Advisor:
Dr. LEE Chee Wee
Associate Professor
Department of Physiology
National University Singapore
Chief Executive Officer
Lynk Biotechnologies Pte Ltd.

Cure for cancer? This could be it

IT WORKED ON HIM: *Associate Professor Lee Chee Wee with one of his test subjects.*

MAGIC BULLET?

The substance which Lynk discovered is potentially a magic bullet, but there's still a lot of work to be done and we have to proceed cautiously.
We have had five or six calls from the public. They requested that this substance be given to their family members who are terminally ill from cancer (of various kinds).
But we had to turn them down because there are still a lot of tests to be done. Though this is an exciting discovery, we have to protect society and test the substance carefully first.

— Dr Gurinder Shahi, CEO of BioEnterprise Asia, which co-founded Lynk

By Dawn Chua

ASSOCIATE Professor Lee Chee Wee is excited.

The chemical substance which his lab discovered recently appears to be very promising in treating cancer.

You see, mice with colon cancer, given a dose of the substance, have recovered from the disease.

Said the founder of Lynk Biotechnologies, the first privately-funded, home-grown, biotech start-up in Singapore:

"It's still too early to tell whether this substance will be effective when used on human beings, but the pre-clinical trials (on the mice) are promising."

Together with his team of 12 scientists, Assoc Prof Lee, 42, came up with the substance about four months ago.

The substance, which is being kept secret for now, forced the tumour cells to change into normal ones.

Said Assoc Prof Lee, who is also with the physiology department of the National University of Singapore's medicine faculty: "The tumours in the mice stopped growing after we injected them with the substance.

"After two weeks, the tumours shrank, meaning we were able to successfully reverse the trend and now, there's zero tumour cell in the mice."

According to standards set by the pharmaceutical industry, it is necessary to wait for seven weeks before anyone can claim that a substance is effective after having tested it on mice.

The seven-week wait for mice is equivalent to five years of a human being's life, and if the mice survive this period, the substance can be said to be effective and not toxic to the mice.

For Assoc Prof Lee and his team, the seven-week wait for the mice to recover was a nail-biting one.

Said Assoc Prof Lee: "We don't know if the mice, which are still alive, have suffered any side effects after the medication. Right now, they're still active and eating well, but we're carrying out tests to check."

But it will take many more years before they know if the substance can be used on human beings, and if so, whether it will be effective.

Assoc Prof Lee explained: "Before we can go into the clinical trial stage, where the substance is available for terminally-ill cancer patients to volunteer to try it, there is about 1½ years of lab work to be done.

It's still too early to tell whether this substance will be effective when used on human beings, but the pre-clinical trials (on the mice) are promising... The tumours in the mice stopped growing after we injected them with the substance. After two weeks, the tumours shrunk, meaning we were able to successfully reverse the trend and now, there's zero tumour cell in the mice.

— Associate Professor Lee Chee Wee

"For instance, we have to document in detail the recommended dosage, side effects (if any) and toxicity levels found in the mice which have been subjected to this treatment.

"Only after this can we make a proposal to the Food and Drug Administration (in the US) for our substance to be used."

This is followed by another waiting period of six to seven years, while the drug is used on patients.

If the patient does not show any signs of relapse for five years, then he is considered cured, and the substance, an effective one.

The next step for Assoc Prof Lee and his team is to test different tumour groups, such as bladder, breast and prostate tumours, on mice, and see if results are similar.

If they do, then the results will strengthen the team's beliefs that this substance might just be the treatment for cancer.

In all, they estimate it will take another 7½ years before the substance, if it is approved, surfaces in the pharmaceutical industry.

Even as numerous tests are being carried out on the substance, Assoc Prof Lee is not counting on the substance to be the next breakthrough in medical history.

He said they are working on other projects too, but can't give details.

"You can't put all your eggs in one basket when it comes to the life sciences — if you bark up a tree and it's the wrong tree, you have to have something else to fall back on, or else your efforts will all be in vain.

"So we have to spread the risk over a few areas."

TheStraitsTimes 23 August 2000

Back

Take a pill and call him in the morning...

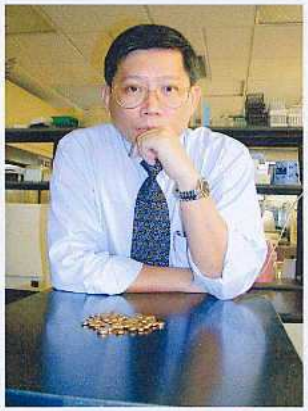
You'll need just one pill a day if this NUS researcher's breakthrough succeeds in making medication more efficient and speeds up drug testing

By CHANG AI-LIEN

A RESEARCHER here has discovered a technique that will speed up the development of new drugs radically and reduce the often-drastic side-effects of many medicines.

In an industry where each drug costs, on average, about US$500 million (S$850 million) to develop and takes 15 years from screening to approval, Associate Professor Lee Chee Wee of the National University of Singapore medicine faculty's department of physiology says he can save millions by slashing at least three years off the development time.

He has set up drug development company Lynk Biotechnologies with life-science incubator MJSS Enterprise Development. They aim to list the company in two years, said MJSS CEO Gurinder Shahi.



When funds are limited, the secret of success lies in taking a narrow, focused approach, says Prof Lee.

Drugs work by attaching or ""binding" themselves to specific proteins found in cells, and switching the functions of these cells on or off.

So, for example, an anti-obesity drug would make fat cells work harder so that a person could lose weight, while an anti-cancer drug could order the cells to stop producing food so cancer cells stop growing.

Prof Lee's breakthrough is in altering drug molecules so that they bind permanently to the cellular proteins and prolong the drug effects, unlike unaltered molecules in conventional medicines, which detach themselves almost immediately.

Thus, lower dosage levels are possible with the new drugs, reducing the side-effects the drug may have.

And since the drug molecules last for about 24 hours in the body, the patient will have to take the drug only once a day.

The method can also be used to test exactly which proteins in cells are targeted by a given drug, out of the millions in the body, said Prof Lee.