

CHAPTER 10.

II. BUCCAL CONTROLLED RELEASE DOSAGE FORMS

A. BUCCAL DOSAGE FORMS

1. PERIODONTAL IMPLANTS
ACTISITE FIBER, ATRIGEL (ATRIDOX)
2. BUCCAL PATCHES
3. GUMS
4. INHALER

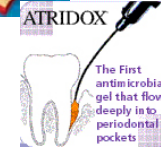
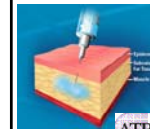
B. FAST-DISSOLVING TABLETS

1. ZYDIS SYSTEM
2. WOWTAB (WITHOUT WATER)
3. QUICKLETS

C. SUPERSONIC POWER INJECTION SYSTEM

ATRIGEL Drug Delivery Systems

<http://www.atrilabs.com/ourtech/atrigel.cfm>



Atridox® / Doxirobe®
Atrix's innovative treatment for periodontal disease, Atridox®, couples an effective antibiotic (doxycycline hyclate, 10.0%) and the Atrigel® drug delivery system to fight the progressive disease before it reached advanced stages. The medicine is applied as a gel to the affected area where it fills the periodontal pocket and solidifies, releasing doxycycline to dramatically reduce bacteria over about seven days. No anesthesia is necessary, and the system containing a bioabsorbable polymer does not have to be removed. Atridox was approved by the U.S. Food and Drug Administration September 4, 1998. Doxirobe is the Atridox equivalent for companion animals marketed by Pharmacia

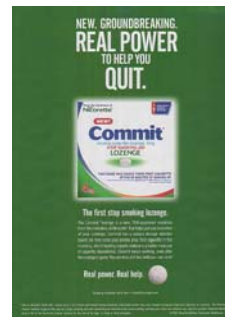
Alternative to ATRIGEL Drug Delivery Systems?

Atrigel:

Sol (Polymer in organic solvent) → Gel

Alternative:

Sol (Polymer in aqueous solution) → Gel



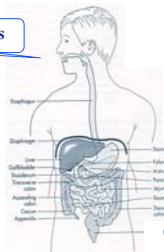
Hand-to-mouth gratification



The Nicotrol Inhaler works by delivering a low dose of nicotine that allows you to reduce your dependence on tobacco. As you bring the inhaler to your mouth and inhale, you breathe in nicotine vapor that is released by the nicotine-filled cartridge in the inhaler. This nicotine is absorbed in your mouth and upper respiratory tract, and not in your lungs.

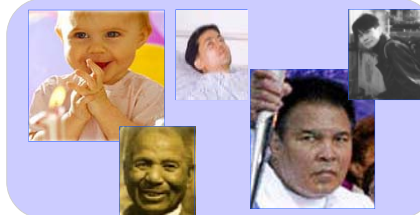
Oral Drug Delivery Technologies

Fast-melting tablets



Pictures from Leon Shargel & Andrew R.C. Yu Applied Biopharmaceutics & Pharmacokinetics, 4th Edn, 1999 Appleton & Lange, Stamford, CT

Fast Melting Tablets



The Existing Technologies

	Advantages	Disadvantages
Freeze Drying	Dissolves within seconds	Highly fragile, expensive
Molding	Low pressure for making tablets	Poor mechanical strength
Sublimation	Higher pressure for making tablets	Use of volatile materials
Direct Compression	High mechanical strength, low cost	Slow disintegration

Representative technology

Company	Technology	Summary	Patent No.
R.P.Scherer	Zydis	Freeze drying	US 5,631,023
Yamanouchi	WOWTAB	Granulation of low moldability sugar with high moldability sugar	US 5,576,014
Cima labs	OraSolv	effervescent (acid + carbonate source)	US 5,178,878
	DuraSolv	Non-direct compression sugar, wicking agent	US 6,024,981
Ethypharm	Flashtab	Multiparticulate tablet	US 6,106,861
Eurand	Ziplets	Water insoluble inorganic particle	WO 99/44580
Fuisz Tech.	Shear form	Candy floss form	US 5,622,719

Commercial Technologies

Zydis® (Cardinal Health)
 OraSolv® (Cima)
 WOWTAB® (Yamanouchi Pharma)
 Frosta® (Akina)
 Ziplets™, AdvaTab™ (Eurand)
 Flashtab® (Ethypharm)
 OraQuick™ (KV Pharmaceutical)
 Pharmaburst™ (SPI Pharma)
 Shear Form (Fuisz Tech)

http://www.kvpharmaceutical.com/tech/3_1_oraquick.html

KV's OraQuick™ system complements our expertise in the area of tastemasking of solid, oral dosage forms.

<http://www.orasure.com/products/default.asp?cid=17&sub=3&sec=3>

The OraQuick® rapid test platform for fingerstick whole blood, has been approved by the FDA for testing for HIV-1 antibodies. The company is working on extending the intended use of the device to other samples like oral fluid and serum/plasma for the presence of various antigens. The device includes a porous pad used to collect an oral fluid specimen. After collection, the pad is inserted into a vial containing a pre-mixed amount of developer solution and allowed to develop.

FDA APPROVES ORASURE ORAL HIV TEST
 The FDA has approved OraSure's Rapid HIV Antibody Test for use with oral fluids, the first rapid oral fluid HIV tests to receive market approval in the U.S.

Commercial Technologies

Zydis® (Cardinal Health)
 OraSolv® (Cima)
 WOWTAB® (Yamanouchi Pharma)
 Frosta® (Akina)
 Ziplets™, AdvaTab™ (Eurand)
 Flashtab® (Ethypharm)
 OraQuick™ (KV Pharmaceutical)
 Pharmaburst™ (SPI Pharma)
 Shear Form (Fuisz Tech)

A solution or suspension of drug is dried into pre-formed blisters

The blisters of product are rapidly frozen by passing through a freeze-tunnel

Frozen product is dried under carefully controlled conditions

Claritin®

Allergy Relief For Your Family

Claritin® Product	Claritin® Tablets	Claritin® 24 Hour Tablets	Claritin-D 24 Hour Tablets	Claritin-D 12 Hour Tablets	Children's Claritin® Syrup
Prescription Strength	✓	✓	✓	✓	✓
Non-Drowsy*	✓	✓	✓	✓	✓
Duration	24 hours	24 hours	24 hours	12 hours	24 hours
Allergy Symptoms Relieved	✓	✓	✓	✓	✓
Age Group	6 years & older	6 years & older	12 years & older	12 years & older	2 years & older

*When used as directed.

Original Prescription Strength

Non-Drowsy*

Claritin RedTabs®

Loratadine Orally Disintegrating Tablets 10 mg/Antihistamine

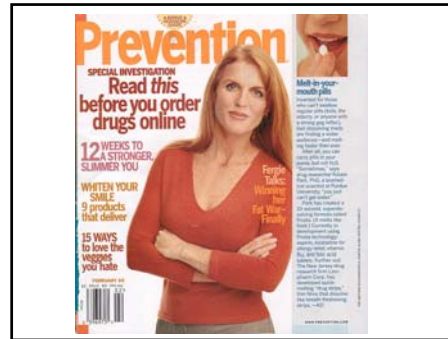
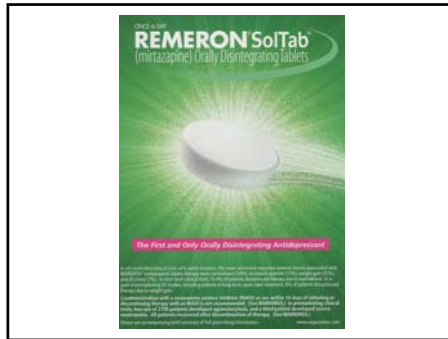
For Adults and Children 6 years and older

24 hour Allergy

Relief of: Sneezing, Runny Nose, Itchy, Watery Eyes, Itchy Throat or Nose

10 ORALLY DISINTEGRATING TABLETS

*When taken as directed-See Drug Facts Panel.



The Existing Technologies

	Advantages	Disadvantages
Freeze Drying	Dissolves within seconds	Highly fragile, expensive
Molding	Low pressure for making tablets	Poor mechanical strength
Sublimation	Higher pressure for making tablets	Use of volatile materials
Direct Compression	High mechanical strength, low cost	Slow disintegration

Fast-melting tablets (dissolving/disintegrating) tablets

Combined benefits of liquid formulation + solid dosage form

Practical Considerations

- Fast melting properties (10-30 seconds)
- Taste & Mouth feel
- High mechanical properties
 - Hardness & Friability (Handling and administration, Multi-tablet packaging)
- Stability (No special packaging processing/materials, Multitablet packaging)
- Easy scale-up processing
- Low manufacturing cost
- Conventional tablet processing

Fast-melting tablets (dissolving/disintegrating) tablets

Combined benefits of liquid formulation + solid dosage form

Practical Considerations

Fast melting properties (10-30 seconds)

- *Fast absorption of water
- *Hydrophilic excipients
- *No blocking of water at the tablet surface

Fast-melting tablets (dissolving/disintegrating) tablets

Combined benefits of liquid formulation + solid dosage form

Practical Considerations

- Fast melting properties (10-30 seconds)
- Taste & Mouth feel

Taste masking of bitter tasting drugs



BETTER THAN ALTOIDS?

Tired of seeing its venerable Listerine mouthwash (first introduced in 1914) getting chewed up in the market by various lozenges, drops and gums, Pfitzer this year introduced Cool Mint Listerine PocketPaks, tissue-thin strips that melt in your mouth and deliver a bracing, breath-freshening punch. They were an instant hit, with more than 100 million sold.

INVENTOR Pfitzer
AVAILABILITY Now, \$1.49 a pack
TO LEARN MORE www.prodhelp.com

TIME, NOVEMBER 18, 2002