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Transdermal Patches: To Cut or Not Cut

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Transdermal drug delivery offers several advantages to patients. The design of the patch allows for both sustained and controlled drug delivery that spans from hours to days. These properties may improve medication compliance – a major concern in patients with multiple disease states especially if they carry a significant pill burden. Bypassing the gastrointestinal system will decrease the risks of local irritation and also increase the bioavailability of drugs that normally undergo significant first pass metabolism.[1, 2] The convenience of this administration route makes it a viable alternative to patients when other routes are less preferred.

Cutting transdermal systems have been a curiosity for both prescribers and patients. Incentives for this practice include manipulation of dose for desired therapeutic effect and control of adverse events. [3, 4] High product costs have also prompted patch cutting as a means of cost-savings comparable to tablet splitting. [5] Even though altering the integrity of the patch may seem logical at first, there are many factors to consider that may influence the efficacy, pharmacokinetics, and safety of the drug.

Patch mechanism and implications of cutting

The underlying mechanism of the transdermal system is based on passive diffusion of the drug from the patch through the skin, and into the circulation for systemic distribution. Fick's Law describes the passage as a constant, zero-order flux rate that is maintained when there is no change in the rate of drug delivery on both sides.[2, 3, 6, 7] The major driver of the concentration gradient is represented by the large quantity of drug within the polymer layer of the patch and smaller quantity beyond the skin. Up to 95% of the total drug amount within some patches has been documented after use.[6, 8] The quantity of drug not only drives the kinetics of delivery but also highlights the importance of proper storage and disposal to avoid accidental overdose.

Some designs allow physical alterations but the proportional relationship between the drug dose and the surface area of patch cannot be ignored.[3, 5, 9] For instance, halving a patch may or may not yield a 50% reduction in delivery and therefore compromise efficacy.[3, 9] On the extreme side, cutting into a drug reservoir may spill out the contents and result in tissue damage or serious toxicity.[5,6] As such, it is important to understand how each different patch system operates to determine if cutting is permissible despite the therapeutic and financial incentives.

Transdermal System Components and Design

General Patch

The basic structural design of the patch system consists of four components – the backing layer, the drug-containing layer, the adhesive layer, and the protective lining. Different patch types have modifications or additions to the basic layers that influences drug storage and delivery, such as the inclusion of a rate-controlling membrane with the reservoir-type systems.

Matrix Type

The polymer binds the drug within the matrix and controls release from the system. The kinetics is pseudo zero-order due to an insignificant decline delivery rate over time. Cutting is possible but may decrease drug efficacy.

Drug-in-Adhesive

A sub-category of the matrix type, this system is based on a homogenous mixture of drug within the polymer adhesive. The approach is done to saturate skin binding sites and so that drug does not have to pass through rate limiting membrane. Cutting patch is possible but may decrease drug amount delivered and efficacy.

Drug Reservoir Type

A rate-controlling membrane placed between the drug matrix reservoir and adhesive to display true zero-order kinetics. There is possible diffusion of the drug into the control membrane over a long period of time which may result in a "burst effect." This event is similar to "dose dumping" from damaged controlled-released oral formulations. Cutting this patch system is **not** permissible.

Micro-Reservoir

A sub-category of the reservoir type, this system uses multiple mini drug reservoirs instead of a single reservoir unit. Cutting patch is possible since only a small number of micro-reservoirs will be destroyed. **However**, the result may alter drug delivery and efficacy.

Drug Reservoir & Heat System

The drug reservoir system is covered with an extra layer that represents the oxygen-activated heating system. Heat is used in this patch type to enhance drug absorption from the skin. Cutting this patch system is **not** permissible. Consequences are similar to other drug reservoir systems.

Drug Reservoir & Iontophoresis

This patch is an integrated, battery-powered, drug reservoir transdermal system. Drug delivery across the skin is facilitated by the application of small electrical currents. Cutting this patch system is **not** permissible.

Table 1: Different Designs of Transdermal Drug Delivery Systems

Matrix Type	Drug Names	Indication	Cutting: Yes, No, Maybe, Unclear
Drug-In-Adhesive Type	**Rivastigmine** (Exelon®)	Mild to moderate dementia of Alzheimer's or Parkinson's disease.	NO
	Diclofenac (Flector®)	Acute sprains, strains, and contusions.	MAYBE
	Estradiol [Alora® Climara® Esclim® Menostar® Vivelle® Vivelle Dot®]	Post-menopausal symptoms.	UNCLEAR
	Estradiol & Levonorgestrel [Climara Pro®]	Moderate to severe vasomotor symptoms associated with menopause.	NO
	Estradiol & Norethindrone [CombiPatch®]	Post-menopausal symptoms.	NO
	Ethinyl Estradiol & Norelgestromin [Ortho Evra®]	Contraception.	NO
	Granisetron [Sancuso®]	Nausea and vomiting for patients receiving some types of chemotherapy.	NO
	Lidocaine [Lidoderm®]	Pain associated with post-herpetic neuralgia.	YES
	Methylphenidate [Daytrana®]	Attention Deficit Hyperactivity Disorder.	NO
	Nitroglycerin [Nitro-Dur ® Minitran®]	Angina pectoris due to coronary artery disease.	MAYBE
	Oxybutynin [Oxytrol®]	Overactive bladder.	MAYBE
	Selegiline [Emsam®]	Major depressive disorder.	NO
Reservoir Type	**Estradiol** [Estraderm®]	Post-menopausal symptoms.	NO
	Fentanyl [Duragesic®]	Persistent moderate to severe chronic pain.	NO
	Nicotine [Nicoderm CQ® Habitrol®]	Smoking cessation.	NO
	Scopolamine [Transderm-Scop®]	Nausea and vomiting from motion sickness.	NO
	Testosterone [Androderm®]	Testosterone replacement therapy.	NO
Micro-Reservoir Type	**Clonidine** [Catapres TTS®]	Hypertension.	MAYBE
Drug Reservoir & Heat System	**Lidocaine & Tetracaine** [Synera®]	Local dermal analgesia for superficial venous access and superficial dermatological procedures.	NO
Drug Reservoir & Iontophoresis	**Fentanyl** [Ionsys®]	Acute postoperative pain in adult patients requiring opioid analgesia during hospitalization.	NO

Yes = Cutting is permissible. No = Do NOT cut. Maybe = Cutting reported in *both* practice and studies. Unclear = Cutting reported in studies *only*.
*Table information adapted from journal articles, FDA drug labels, product manufacturer and consult with Zhengrong Cui, Ph.D. from Oregon State University.

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References:

1. Buxton Iain L, "Chapter 1. Pharmacokinetics and Pharmacodynamics: The Dynamics of Drug Absorption, Distribution, Action, and Elimination" (Chapter). Brunton LL, Lazo JS, Parker KL: Goodman & Gilman's The Pharmacological Basis of Therapeutics, 11th Edition: http://www.accessmedicine.com/content.aspx?aID=935800.
2. Scheindlin S. Transdermal drug delivery: past, present, future. Molec Interv. 2004; 4: 308-312.
3. Lee HA, Anderson PO. Giving partial doses of transdermal patches. Am J Health-Syst Pharm. 1997; 54: 1759-1760.
4. Dmochowski RR, Starkman JS, Davila GW. Transdermal drug delivery treatment for overactive bladder. Internationl Braz J Urol. 2006; 32: 513-520.
5. Ball AM, Smith KM. Optimizing transdermal drug therapy. Am J Health-Syst Pharm. 2008; 565: 1337-1346.
6. Mehta R. Topical and transdermal drug delivery: what a pharmacist needs to know. Available at: www.inetce.com/articles/pdf/146-000-01-008-h01.pdf. Accessed October 10, 2008.
7. Naik A, Kalia YN, Guy RH. Transdermal drug delivery: overcoming the skin's barrier function. PSTT. 2000; 3: 318-326.
8. Pasero C, McCaffery M. The lidocaine patch. Amer J Nursing. 2001; 10: 22-23.
9. Tom WC. Characteristics of transdermal patches. Pharmacist's Letter/Prescribers' Letter. 2008; 24: 240711.