

# *Drug Delivery Market Summary*

## **Drug Delivery Summary**

Silicones have been cited as materials regularly used in drug delivery devices. These drug delivery devices incorporating silicones primarily fall into three major categories:

- Implanted delivery devices
- Mucosal delivery devices
- Transdermal delivery devices

Implanted drug delivery devices include spinal treatment devices, ocular treatment devices and contraceptive devices. These delivery configurations typically utilize silicone tubing or molded configurations. The silicone is used to either hold or precisely deliver the drug to a specific location. Liquid silicone rubbers or high consistency silicone rubbers can be molded into precise configurations required by these applications.

Transmucosal drug delivery devices can include silicone elastomer systems with the drug incorporated into the silicone matrix. After the device is placed in contact with the mucosal membrane, the drug elutes from the device at a controlled rate. A non-medicated sheath is cited (References 12,11,7) as a means to control the initial burst of drug from the device. Drugs can be incorporated into liquid silicone rubbers and molded into various configurations.

Transdermal delivery devices are primarily skin patches in configuration. The drug may be incorporated directly into the adhesive of the patch or may exist as a separate layer. Silicone pressure sensitive adhesives have been used in these applications because of the low skin sensitization, oxygen and drug permeability properties they offer. Silicone materials used in medical device configurations can also be treated with drug infused coatings.

## **Materials**

NuSil Technology offers a complete line of off the shelf silicones and offers customized versions of the following materials types:

<b>Silicone Type</b>	<b>Application</b>
Liquid Silicone Rubber	Molded Parts
High Consistency Rubbers	Molded Parts, Extruded Tubing
Pressure Sensitive Adhesives, Gels	Temporary Adhesives

Two types of liquid silicone rubbers are cited as candidates for transmucosal drug delivery systems, non-acetoxy RTV silicones and platinum catalyzed silicones.

## Drugs or Active Agents

The table below is a list of drugs cited (References 5-14) as candidates for incorporation into a silicone transmucosal drug delivery device. These same citations list typical amounts of 5 to 15% by weight of the drug for release rates of 10 to 500 micrograms per day in a 30 to 60 day time frame. Rate enhancing additives can improve release rates significantly (Reference 9) and are listed below the table. Release rates are essentially zero order. Particle sizes, where applicable, are cited as below 200 microns for the most effective release rates. References for these drugs are listed in the references section under transmucosal drug delivery.

<b>Indication Category</b>	<b>Active Ingredient</b>
Antidepressants / Anxiolytics	17.beta.-estradiol Progesterone Medroxyprogesterone Norethisterone Trimegestrone Noretheristerone acetate Mifepristone Ethinyl estradiol
Anxiolytics	Fluphenazine Flupenthixol Haloperidol Buspirone Alprazolam Trifluoperazine
Vitamin B6	Pyridoxine Pyridoxal Pyridoxamine
Vitamin D	Cholecalciferol Dihydrotachysterol Ergocalciferol Alfacalcidol
Vitamin E	d-alpha Tocopherol
Opioid Analgesics	Buprenorfine Levorphanol Phenoperidine Fentanyl Methadone
Non-Opioid Analgesics	Mefanamic Acids
Antiviral	Acyclovir Vidarabine Arildone Idoxuridine Cestrinone Mifepristone
Antifungal	Clotrimazole Enconazole Iitraconazole Metronidazole

## Rate Enhancing Additives

Silicone polymers are relatively hydrophobic and it's thought the list of compounds below can increase the rate of release. The typical amount by weight added to the elastomer system is cited at 5 to 20%.

<b>Rate Enhancing Additives</b>
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Fatty acid esters – Isopropyl myristate Caproic acid Lauric acid Oleic acid Linoleic acid Adipic acid Lanolic acids
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## NuSil Technology / Drug Delivery

NuSil Technology is actively involved in the development of custom materials for the drug delivery industry. Our customers range in size from Fortune 500 to start-up ventures. NuSil's focus on silicone materials and chemistry can help customers prototype devices quickly. We have worked extensively with major pharmaceutical customers to supply materials for several commercially successful drug delivery devices on the market today.

Please contact a NuSil Technology technical sales representative regarding additional resources on silicone's use in drug delivery applications at 805-684-8780.

## References

### Transdermal Drug Delivery:

- (1) Woodward, J.T and Metevia, V.L. Transdermal Drug Delivery Devices with Amine-Resistant Silicone. U.S. Patent 4,655,767
- (2) Studen, J.R., Method and Composition for the Treatment of Scars. U.S. Patent 6,337,076

### Implanted Drug Delivery Devices:

- (3) Segal, M., Patches, Pumps, and Timed Release *FDA Consumer* (October 1991)
- (4) DiCosmo, F. and Ditzio and Valerio Drug Delivery via Therapeutic Hydrogels U.S. Patent 6,228,393

### Transmucosal Drug Delivery Devices:

- (5) Woolfson AD, Malcolm RK, Gallagher R (2000) *Ther. Drug Del. Carr. Sys.*, 17, 509-555
- (6) McCullagh, SD, Woolfson AD, Malcolm RK, Gallagher R (2001) *Novel Silicone Crosslinkers for Intravaginal Drug Delivery* British Pharmaceutical Conference Abstract Book:91
- (7) Nabahi, Shorhe Intravaginal Drug Delivery Device U.S. Patent 6,039,968
- (8) Malcolm RK, Woolfson AD, Elliott G, Shepard M Intravaginal Drug Delivery Devices for the Administration of an Antimicrobial Agent U.S. Patent Application 2030059456
- (9) McClay A Intravaginal Drug Delivery Devices for the Administration of 17.bets.-oestradiol Precursors U.S. Patent Number 5,855,906
- (10) Zimmerman I, Windt F, Reck HJ Vaginal Ring U.S. Patent 4,822,616
- (11) Passmore C, Gilligan C Intravaginal Drug Delivery for the Administration of Testosterone and Testosterone Precursors U.S. Patent 6,416,780
- (12) Nabahi, Shorhe Intravaginal Drug Delivery Device U.S. Patent 6,103,256
- (13) Nabahi, Shorhe Intravaginal Drug Delivery Device U.S. Patent 5,788,980
- (14) Saleh SI, Nash HA, Bardin WC, Harmon T Intravaginal Rings with Insertable Drug Containing Core U.S. Patent 6,126,958



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