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Literature Review: Silicone Applications in Health Care

INTRODUCTION

Early in the 20th century, the term 'silicone' was coined by Professor Frederic Stanley Kipping, a British chemist and one of the founding fathers of silicon chemistry [8,16]. The word was given to describe new compounds containing a Si-O linkage (siloxane bond) and basic chemical formula R_2-Si-O [8]. In industry, silicone usually refers to linear polydimethylsiloxane (PDMS), the most basic silicone polymer containing only methyl groups as substituents in the polymeric structure (Figure 1) [8]. However, the term silicone can also be used to describe complex polymer structures that feature a wide range of functional groups, branching or crosslinking [8]. "The properties of basic PDMS materials can be changed by replacing some methyl groups with other organic groups or atoms [10]." Substitution of this type is useful when specific physical and chemical properties are required of the material, such as adhesion or compatibility with a certain substrate [10]. Since their discovery in the 1900s, silicones have been incorporated into a vast number processes and fields such as:

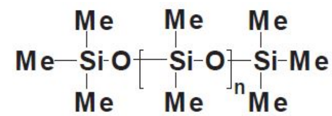

Figure 1: The chemical structure of polydimethylsiloxane (PDMS) [10]

- Chemicals
- Coatings
- Construction/maintenance
- Electrical
- Electronics/photonics
- Food
- Medical and pharmaceutical
- Mold-making
- Personal care
- Plastics
- Pressure sensitive adhesions
- Pulp and paper
- Textiles
- Transportation systems

This review will look specifically at the applications of PDMS-based materials in the medical and pharmaceutical industries. The first use of silicone in health care dates back to 1956, with the invention of a silicone elastomeric tube for hydrocephalic shunt procedures [9]. The development of the tube was a collaborative effort of two medical doctors and scientists from the Dow Corning Corporation [9]. Today many permanent internal devices, medical instruments, health care products and pharmaceuticals use silicone as their base material [9].

PDMS is a highly hydrophobic compound with several unique properties that make it perfect for biological purposes. In the text *Polymeric Biomaterials,* PDMS is said to be "chemically stable under physiologic conditions, can be synthesized with a variety of physical properties, and … molded easily [9]." This polymer can be synthesized in elastomeric form when partially crosslinked or as a gel. A gel has the same structure as an elastomer but at a much lower crosslink density [17]. Additionally, gels are usually swollen with a fluid [9,17]. Because PDMS has a very low specific gravity (lower than that of water) and is chemically inert, it is the most common fluid used in medical applications [9].

Biocompatibility is the fundamental property of a material that needs to be considered before it can be used in medical applications. In the *Concise Encyclopedia of High Performance*

Silicones, D.F. Williams describes biocompatibility as, "the ability of a biomaterial to perform its desired function with respect to a medical therapy, without eliciting any undesirable local or systemic effects in the recipient or beneficiary of that therapy, but generating the most appropriate beneficial cellular or tissue response in that specific situation, and optimizing the clinically relevant performance of that therapy [17]." From a research standpoint, there is a list of reactions that must not occur when the potential biomaterial is tested. Those prerequisites include the absence of toxic/allergic/inflammatory reactions, no destruction of formed elements, no immunological reactions, no carcinogenic effects, and no deterioration of adjacent tissue [1]. PDMS materials are shown to comply with these requirements as well as display properties such as hemocompatibility [17]. For these reasons PDMS continues to be the most widely used silicone in health care [6].

APPLICATIONS OF PDMS

The U.S. Food and Drug Administration acknowledge PDMS as a biocompatible material under the trade name dimethicone for its hydrophobicity, low surface tension, and spreading properties [10]. As mentioned previously, the material can be used in the form of a fluid, gel, elastomer, or compound [10]. This review will delve into these different systems and demonstrate their effectiveness in four biomedical applications: lubrication, protection, implantation and active ingredient delivery.

PDMS Fluids

Due to the non-hindering methyl groups in the linear PDMS structure (Figure 1), the polymer chains are able to slide past one another, making it a great fluid for lubrication or siliconization. The latter, a process often used to decrease gliding forces in syringes, helps to ensure a smooth injection of a product by reducing the friction between the syringe plunger and the barrel surface [17]. Methods of siliconization have improved over the years, ensuring that the silicone oil coating does not leach into the substance contained within the syringe [17]. The current method involves spraying a silicone emulsion into a pre-cleaned syringe and then heating the substrate to 300°C for 15-30 minutes. There are many parameters that must be considered during the siliconization process such as spray volume, emulsion concentration, oven temperature, heat exposure time, etc. [17]. This method of "baking in the siliconization process has resulted in a significant improvement in the physical stability of silicone coatings [17]."

In addition to the siliconization of syringes, personal lubricates and condoms are another area of health care where PDMS fluids are incorporated [10]. In a study done by the University of Technology in Sydney, Australia, researchers analyzed 58 condoms by 10 different brands for lubrication type [11]. Their analysis included fluorescence light microscopy, diffuse reflectance infrared Fourier transform spectroscopy (DRIFTS), gas chromatography/mass spectrometry (GC/MS), and pyrolysis gas

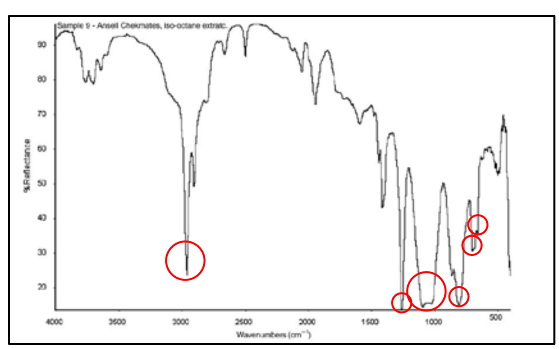

Figure 2: DRIFTS analysis of a condom showing the presence of PDMS [11]

chromatography/mass spectrometry (PGC/MS) [11]. From their study, they found that 20 of the 58 condoms use PDMS as their base lubricant [11]. The detection of PDMS was indicated by the presence of peaks in DRIFTS analysis at 3000-2850, 1260, 1100, 1020, 860 and 810 cm^{-1} as shown in Figure 2 [11]. In addition to this study, a premarket notification from the FDA details the components of several Trojan™ brand personal lubricants in which dimethicone is a main ingredient [13].

Both aforementioned uses of PDMS as a lubrication material demonstrate the effectiveness of this polymer as a fluid in health care applications. Because of its low surface tension, which promotes good wetting of most solid surfaces [17], "polydimethylsiloxane … is the most commonly used fluid in medical practice [9]."

PDMS Gels

PDMS gels are partially crosslinked polysiloxanes networks that are swollen with a silicone fluid [9]. Silicone gels have been found to be very successful when used as wound dressings due to their soft, rubbery nature [2]. These properties make them appropriate materials for an interface to biological tissues because they are capable of minimizing the risk of trauma at the site [2]. The use of silicones in wound care dates back to the early 1960s where silicone fluids were used as immersion treatments for burn patients [18]. It is important that wound care materials have low skin stripping force, gentle removability and the lack of adhesion to wound beds. These properties are inherent of PDMS gel materials [2]. In addition, PDMS gels are permeable which is important in wound care [2,10]. Permeability allows for the diffusion of gases such as oxygen, carbon dioxide or water vapor out of a wound, and the movement of plant extracts, drugs or even proteins in [2]. Wound dressings are particularly important in burn injuries due to the likelihood of scar formation. According to the journal *Burns,* "the development of hypertrophic scarring is one of the most common and frustrating problems after burn injury, due to its functional and aesthetic consequences [18]." Hypertrophic scars present as a red to deep purple scar which can become elevated, firm or hypersensitive as healing occurs [18]. In the last decade, silicone gel sheets as drug releasing media have been increasingly incorporated into wound protocol for hypertrophic scarring [18]. Common active pharmaceutical ingredients (APIs) for these gel sheets are vitamin E or topical antimicrobial agents [18]. Silicone gels sheets have been shown to induce hydration of hypertrophic scars and keloids, allowing for the regeneration of healthy tissue and the reduction of scar elevation [3]. Although the mechanism for this process is still unknown, it could be due to the inhibiting effect that hydration has on fibroblasts that produce collagen [3]. In addition, silicone gel sheets have "been shown efficacious not only in the treatment but also in the prevention of [hypertrophic scars] and [keloids]. The application of [silicone gel sheets] after surgical resection prevented the development of [hypertrophic scars] and [keloids] in 75% to 85% of the cases [3]."

Figure 3: CICA-CARE silicone gel sheet for wound and scar treatment [5]

In the application of wound care, PDMS gels can be used as both a protective barrier and as an active ingredient delivery system because of their permeability, lack of adhesion to open wound sites and smooth, skin-like texture [8].

PDMS Elastomers

Silicone polymers can be converted into elastomeric materials by creating crosslinks in the form of covalent bonds between adjacent macromolecules [8]. The resulting three-dimensional network can be used as thin films, implantations, adhesives or as materials in other health and personal care applications [2,10]. Commercially available PDMS is manufactured as elastomers (also known as "gums") rather than as fluids or gels [9]. The difference between PDMS elastomers and fluids or gels is the polymers' ability to stretch when elongated and its immediate recoil upon the reduction of tension. "A lightly crosslinked polymer [elastomer] will deform easily but will have significant elasticity, with the ability to return to its original shape when stress is released [9]."

In 1960, the first silicone breast implants were developed by Dow Corning Corporation in collaboration with two surgeons who wanted to find a material for mastectomy patients that would not harden or change shape over time [9]. The resulting "mammary prosthesis" was a silicone rubber sac filled with silicone gel [9]. Over the years, the demand for mammary prosthesis implants for both cosmetic and reconstructive patients has increased dramatically, becoming a multimillion dollar product [9]. In the text *Polymeric Biomaterials,* it was estimated that in the year 1992, 1-2.5 million North American women received breast implants [9]. After the rise in breast implants began, researchers began linking silicone implants with connective tissue disease; however, in 1994 "a Department of Health advisory group in Great Britain reported that there was no evidence of an increased risk of connective tissue disease in patients with silicone breast implants [9]." Studies revealed that the risk was no different than the risk among the general population [9]. In 1996, an article published in the *Journal of the American Medical Association* concluded that a link between connective tissue disease and silicone breast implants was unlikely [9]. There are currently five silicone gel-filled breast implants that are approved by the FDA; the implant displayed in Figure 4 is made by a company called Allergan [14]. The device is composed of a dimethyl silicone elastomer shell and filled with a silicone gel [15].

Figure 4: Inamed® Silicone-Filled Breast Implants by Allergan [4]

An important feature of any biomaterial used in implantation is the ease of surface modification to eliminate the risk of microbial colonization and infection [17]. "Hydrophobic surfaces tend to adsorb proteins from the surrounding biological environment, subsequently triggering microbial adhesion and biofilm formation [17]." The accumulation of such responses can lead to the body rejecting the implant [17]. Because of the tailorable functionality of silicones, they are overwhelmingly used as biomaterials in implantation procedures. In addition to mammary prostheses, other PDMS based implants include blood pumps, cardiac pacemaker leads, drainage implants for glaucoma, artificial skin, maxillofacial reconstruction, replacement esophagus, finger joints, coating for cochlear implants and catheters [1].

PDMS Compounds

PDMS can be compounded with other materials such as filler to change the properties of the final product. One example of a PDMS compound is simethicone, a blend of polydimethylsiloxane and silicon dioxide [7]. This product is used in gastroenterology for its antifoaming properties [8]. A simethicone formulation will frequently contain 90.5 – 99.0%

Figure 5: Mylanta antiflatulent medication which contains 125mg Simethicone [12]

linear PDMS and 4.0 – 7.0% silicon dioxide [7]. This compound is used to reduce foaming in the gut without modifying gastric pH levels [8]. Simethicone is used as an API or an excipient in many antiflatulent or antacid drugs [7]. In fact, "this is the largest single application for silicones," with 64 registered products including common over the counter medications such as Maalox® and Mylanta® [7]. In addition to silica, simethicone can be compounded with other active ingredients such as aluminum- or magnesium hydroxides, as well as magnesium- or calcium carbonates which can further reduce acid production in antacid formulations [7].

Sunscreen is a personal care product that will often utilize elastomeric PDMS as a delivery agent for APIs [10]. In this respect, the elastomer-API material is also classified as a compound. The addition of dimethicone elastomer to octyl methoxycinnamate, a sun screening chemical, increases the product's sun protection factor (SPF) significantly [10]. One study compared a 4% silicone elastomer (Dow Corning® 9040 Silicone Elastomer Blend) to a control product without elastomer. The results showed that the elastomer presence increased the SPF from 5.7 to 18.0 (Figure 6) [10]. "As a result, formulation costs can be reduced along with potential irritation caused by sunscreen additives," writes Paal Klykken et al. in *Silicone Film-Forming Technologies for Health Care Applications.*

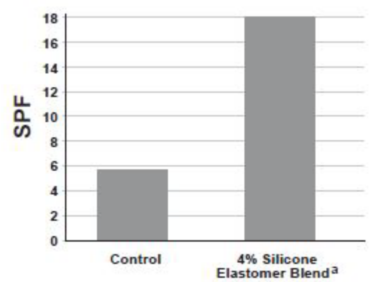

Figure 6: Sun protection factor study that demonstrated that the addition of a silicone elastomer blend to a sun care formula increased the SPF from 5.7 to 18.0 [10]
[a]Dow Corning® 9040 Silicone Elastomer Blend

In both compound PDMS formulations presented, the polymer is used as a delivery agent for active pharmaceutical ingredients because of PDMS' biocompatibility and chemical inertness [17].

CONCLUSION

Polydimethylsiloxane, generally known as silicone, is used in applications requiring biocompatibility because of its "physiological inertness, low toxicity, good thermal stability and anti-adhesive properties [17]." PDMS systems have been shown effective in many biomedical applications including lubrication, protection, implantation and active pharmaceutical ingredient delivery because of inherent characteristics of the polymer. Table 1 lists some of these features, taken from the *Concise Encyclopedia of High Performance Silicones.*

Table 1: Notable properties of polydimethylsiloxane (PDMS) [17]

Biological	Physiochemical	
Non-toxic	Thermal stability	Low density and high molecular weight
Inert	Resistance to UV, oxygen, ozone and sunlight	Chemical stability
Biocompatibility	Resistance to aging and biodegradation	Flexibility / Elastic, easy to mold and shape
Hemocompatibility	Can be sterilized	High gas permeability
	Excellent dielectric behavior	Good optical transparency
	Low curing temperatures	Hydrophobic character

Because of PDMS' many favorable properties, silicones are used in numerous health care applications, both internal and external to the human body. Among internal applications are prosthetic heart valves, orthopedic implants, cardiac pacemakers, vascular prostheses, urinary catheters, voice prostheses, maxillofacial prostheses, ocular prostheses, intrauterine contraceptive devices, contact lenses, drug delivery systems, and breast implants [17]. External applications include wound and scar treatments, tissue engineering scaffolds, and personal care products like sunscreen, antiflatulents or personal lubricants [8,9]. As time progresses, the list of silicone applications in the medical and pharmaceutical fields continue to increase. It is evident from the spectrum of uses that polydimethylsiloxane materials are tremendously important to the prolonged advancement of health care technology.

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