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Silicone-based biomaterials for biomedical applications: antimicrobial strategies and 1 **3D** printing technologies 2 3 Mina Zare^{1*}, Erfan Rezvani Ghomi¹, Prabhuraj D. Venkatraman² and Seeram Ramakrishna^{1*} 4 ¹Center for Nanotechnology and Sustainability, Department of Mechanical Engineering, 5 National University of Singapore, Singapore 117576, Singapore 6 ² Faculty of Arts and Humanities, Manchester Metropolitan University, Manchester M156BG 7 8 UK 9 Corresponding author: seeram@nus.edu.sg, zare.mina@yahoo.com 10 Abstrac Silicone is a synthetic polymer widely used in the biomedical industry as implantable devices since 11

12 1940, owing to its excellent mechanical properties and biocompatibility. Silicone biomaterials are renowned for their biocompatibility due to their inert nature and hydrophobic surface. A timeline 13 14 illustration shows critical development periods of using silicone in varied biomedical applications. 15 In this review, silicone properties are discussed along with several biomedical applications, including medical inserts, speciality contact lenses, drains and shunts, urinary catheters, 16 17 reconstructive gel fillers, craniofacial prosthesis, nerve conduits, and metatarsophalangeal joint 18 implants. Silicones are prone to microbial infections when exposed and interactions with the host 19 tissue. As in the case of medical inserts, the development of specific antimicrobial strategies is 20 essential. The review highlights silicone implants' interaction with soft and bone tissue and various 21 antimicrobial strategies, including surface coating, physical or chemical modifications, treating 22 with antibiotics or plasma-activated surfaces to develop the resistance to bacterial infection. 23 Finally, 3D printing technology, tissue engineering, regenerative medicine applications, and future 24 trends are also critically presented, indicating the silicone's potential as a biomaterial.

25 1 Introduction

Silicone or polysiloxane is a synthetic polymer widely used in biomedical applications. It is made 26 up of silicon, oxygen, carbon, and hydrogen. The material is a mixture of semi-inorganic polymeric 27 28 molecules consisting of an array of polydimethylsiloxane [(CH₃)₂-SiO] monomers chains of 29 different length ¹. The physical property of silicone is determined by the average length and the degree of cross-linking between its polymer chains. The highly ionic Si-O bond results in high 30 bond strength, thus giving silicone its high thermal and chemical stability. Fig. 1 shows a synthesis 31 of a common form of silicone (polydimethylsiloxane (PDMS) with chemical structure ². Fig. 2 32 33 displays some of the key milestones in silicone development as well as its application as a 34 biomaterial.

35 1.1 Properties of Silicone

36 Silicone polymers are versatile and can be formulated into various distinct material types,

- including elastomers, gels, adhesives, and more, depending on the intended application. One of
 the standout properties of silicone is its low glass-transition temperature at approximately -120°C,
- 39 enabling the material to retain its flexibility at extreme temperature conditions, for example, in

1 cold storage. Some other critical physical properties of silicone are high elasticity and high 2 hydrophobicity, with a water contact angle of 101° to 109°. Table 1 summarises a few fundamental 3 properties of PDMS compared to other common soft polymers¹. One of the advantages of silicones 4 is their ability to maintain their mechanical properties from -40° C to $+185^{\circ}$ C. Silicone elastomers 5 are available in a wide range of hardness, have good UV resistance, excellent thermal and chemical 6 resistance. Also, it possesses good electrical properties, flame resistant, and allows sterilisation 7 using steam, autoclave, or gamma radiation². Silicone is highly permeable to gases, optically 8 transparent, and easy to manufacture³. Silicone is very versatile and can be formulated into various 9 forms, depending on its intended applications. Silicone elastomers are widely used in medical 10 device applications. Below are some of the common forms of silicone-based materials¹.

- Silicone elastomer
- Silicone gel

11

12

13

Silicone adhesive

14 *1.2 Biocompatibility and Biodurability*

15 Silicone is highly biocompatible and bio-durable when interacting with host tissues. The 16 hydrophobicity and low surface tension of silicone results in high hemocompatibility and reduces potential contacting 17 of encrustation when the various the body fluids ^{4,5}. Silicone is also generally unaffected by host tissue attack and repeated sterilisation due 18 to its widely recognised chemical and thermal stability⁵. These properties favour the use of silicone 19 biomaterial in various biomedical applications. Silicone elastomer is used as tubing for catheters 20 or drains that requires it to be transparent, flexible, inert, lubricant, and biocompatible; insulation 21 for electronic implants (pacemaker leads). Silicone adhesive or elastomer is also used for wound 22 23 dressing because it is biocompatible, comfortable, and allows air permeability. Silicone gel is used 24 in the treatment of hypertrophic burn scars 6 , whilst silicone rubber is widely used in prosthesis 2 .

25 **2** Biomedical Applications of Silicone

The silicone applications range from extracorporeal equipment, catheters, drains, shunts, various long-term implants, orthopaedic implants, and aesthetic implants⁷. The following section provides a critical discussion of various biomedical devices applications, highlighting silicone material properties and the antimicrobial strategies for each application. The diverse applications of silicone are given below ^{4,5}.

- Coating, treatment, or assembly of various medical devices
- Inserts and implants to replace various body parts
- Catheters, drains, and shunts used for medical treatment and short-term implant
- Aesthetic implants
- Specialty contact lenses

Table 2 demonstrates diverse examples of silicone implants in various locations in the human body. Silicone can be inserted into almost every part of the human body, highlighting its great versatility and biocompatibility owing to its hydrophobicity and inertness. Some key functional properties of silicone are listed below ^{5,8}.

- 40 Silicone elastomers are relatively firm and flexible.
- Form stability under a wide range of temperature and chemical conditions.

- 1 Hemocompatibility due to its hydrophobicity, thus retaining blood properties.
 - Silicone has a high permeability to gases, including oxygen, carbon dioxide and moisture.
 - It is inert, non-toxic, and nonbiodegradable.

4 2.1 Silicone in Biomedical Devices

2

3

5 Silicone surface treatment on glassware and needles helps to preserve blood from clotting for a 6 longer period². Researchers at the Mayo Clinic demonstrated during 1949 that blood has 7 insignificant changes in coagulation time after being left in silicone-coated syringes⁵. Silicone precoated needle reduces pain, which was evident in the penetration force diagram (Fig. 3)⁸. Silicone 8 9 coating significantly reduces the load when the needle penetrates the skin surface, indicating 10 greater ease of penetration, explaining patients' less pain. Since then, silicone is used as a coating 11 for needles, syringes, and blood collection vials. The purpose of precoating is to leverage silicone's 12 favourable surface properties onto these medical devices, such as its ability to preserve blood and 13 lubricating ability, which reduces insertion force. Silicone tubing and membranes are also widely 14 used in kidney dialysis, blood-oxygenator, heart-bypass machines, and heart valves. Silicone 15 tubing is preferred in these applications again due to its stability, hemocompatibility, and high 16 oxygen permeability required when transporting body fluids 2,4 .

17 2.2 Silicone as Medical Inserts and Implants

18 It is interesting to note that Frank H. Lahey was the first to report silicone elastomer implant in

- 19 humans. In April 1946, he reported that 'bouncing clay' was used to repair bile ducts. In 1948, Dr.
- 20 DeNicola completed the first human male urethra replacement by threading a 9.5cm long silicone

21 tube through catheterisation. Another significant milestone was developing silicone finger joint

22 implants by Dr. Alfred Swanson in 1968, with support from Dow Corning, where silicone was

used as a spacer to replace cartilage function and soft tissue at the finger joints. In 1969, silicone

24 was also adopted in the total knee replacement, functioning as a shock absorber between the tibial

25 and femoral components 5 .

Implants made of silicone is widely used in various location in the human body. Table 2 illustrates 26 27 some examples. The primary purpose of these inserts and implants is to repair the damaged body 28 parts such as tracts and soft bones. Fig. 4 illustrates the treatment of arthritis, where a silicone 29 implant is inserted in finger joints to replace the function of cartilage, which is a firm but flexible 30 connective tissue, much like the properties of silicone. The versatility of silicone implants is 31 mainly due to their high elasticity, chemical, and thermal stability. Silicone is also inert to body 32 fluids and nontoxic, which resulted in it being very suitable for long-term implantation without 33 adverse biocompatibility and biodurability complications ^{6,7}.

34 2.3 Silicone Speciality Contact Lenses

35 Silicone hydrogel lenses were first introduced to the market relatively in 1998, in which they were 36 specially designed for continuous wear to facilitate the recovery from ocular tissue injuries. 37 Between October 2000 and April 2002, a clinical trial with 70 patients with various eye conditions 38 conducted in the Department of Ophthalmology of the Medical University of Warsaw. The results showed that silicone hydrogel lenses were effective as therapeutic lenses where 91% of patients 39 over 18 months reported improvement ⁶. None of them reported any adverse condition ⁶. 40 Yesilirmak et al. reported in 2013 that patients reported no infection after seven years of continuous 41 wear with daily antibiotic drops ⁹. Silicone contact lenses can achieve such breakthrough in 42

1 continuous wear, mainly due to their high oxygen permeability, which is 5 to 10 times higher than 2 typical disposable hydrogel lenses. It also has a favourable bacterial property which significantly 3 reduces the possibility of bacterial infection ¹⁰. To correct the vision of the wearer, contact lenses 4 are used. When worn, the contact lens interacts with the corneal, conjunctival epithelia, and the 5 ocular surface tear film. Silicone can be used in the fabrication of contact lenses in the form of 6 silicone hydrogel which weapfirst interacts the market in 1000 &?

6 silicone hydrogel, which was first introduced into the market in 1999 8,9 .

Silicone has excellent oxygen solubility and low chemical reactivity, allowing it to retain hydrogels positive attribute when incorporated with the soft lens. However, silicone is hydrophobic by nature and can cause discomfort to the user through the destabilisation of the tear film ¹². A hydrophobic lens can also lead to the accumulation of deposits on the lens; thus, modification is required for silicone hydrogel to be compatible with the ocular surface. Typical modification includes surface treatment or the application of a soluble polymer in the material to produce an interface between the tear film and the lens ^{11,12}.

15 produce an interface between the tear finin and the felis .

14 The incorporation of siloxane with soft contact lens material increases the contact lens oxygen 15 permeability compared to a conventional contact lens, as summarised in Table 3. The increase in 16 oxygen permeability allows silicone hydrogel contact lenses to be worn for a more extended period

17 than conventional contact lenses 13,14 . Besides extending the wear capabilities, the use of silicone

18 hydrogel contact lenses leads to fewer complications when compared to conventional contact lens

19 such as eliminating lens-induced hypoxia in the most wearer and reducing the stress-induced

20 corneal homeostasis compared to conventional contact lenses ^{12,14}. Despite its advantage, users of

- 21 silicone hydrogel contact lenses are still susceptible to irreversible effects on corneal homeostasis
- 22 from prolonged use of contact lenses. Also, the high elastic modulus of silicone hydrogel lens can
- 23 lead to a more significant mechanical abrasion impact on the corneal surface than the conventional

24 lens, which can be minimised by optimising the lens design 12 .

25 2.4 Drains and Shunts

26 A shunt is a flexible tube used to drain the brain's excess fluid, usually in the brain's lateral 27 ventricles. Hydrocephalus is a condition that causes the head to swell due to the build-up of 28 cerebrospinal fluid in the brain. The shunt is a medical device that consists of three components -29 inflow or proximal catheter that drains the cerebrospinal fluid from the lateral ventricles; a valve 30 mechanism that regulates the pressure by controlling the fluid flow in the tubing; and the third part is the outflow or distal catheter that drains the cerebrospinal fluid to the abdominal cavity or 31 suitable drainage site ¹⁵. Casey Holter, a months-old baby, suffered from this condition. A shunt 32 33 catheter was implanted made of polyethylene, which did not have a valve to prevent backflow. 34 This was later rectified using a silicone elastomer supplied by Dow Corning. The first successful 35 implant of Holter Shunt was completed in March 1956 and is still in use saving many children from this health condition which, if not treated in time, will cause brain damage (Fig. 5)¹⁶. A 36 37 surgical drain is a thin and flexible tube but is mainly used to drain fluids such as pus and blood 38 out from the body. On the other hand, a shunt is a passage that facilitates movement from one part 39 of the body to another and is usually a more complicated system that requires valves to control the direction of fluid movement. ^{5,17}. 40

41 *2.5 Urinary catheter*

A catheter is a thin and flexible tube that is used commonly in medical treatment for various
 purposes. Urinary catheters can be used for urine drainage from the bladder for patients with a

physical obstruction that obstructs urine flow, faulty bladder muscles or nerves, incontinence, and unconscious patients. They can also be used to measure urine from patients who are incapacitated or young children that are not toilet trained and obtained a clean urine sample that is uncontaminated ¹⁸. It is inserted into a body cavity, duct or vessel to allow draining or administration of fluids ¹⁸. Some common examples are urinary catheter and peritoneal Catheter ^{7,19}.

7 A catheter can be made from various materials or combinations such as silicone, latex rubber, or 8 polyvinyl chloride (PVC). The choice of material can depend on various factors such as the specific 9 application and the intended duration in situ. As shown in Table 4, silicone is inert and can be used without any lubrication yet achieve the longest time in situ¹⁹. Also, the hydrophobicity of silicone 10 11 surface limits encrustation, which again explains its suitability for long-term usage. Silicone adhesive also adheres well to the skin and does not cause irritation, and possesses good 12 permeability to gasses and moisture ⁵. Silicone's biocompatibility, modest resistance to abrasion, 13 low surface tension, good thermal and chemical stability make it the ideal choice²⁰. Numerous 14 15 urinary catheter variations are available in the market; however, specific attention is offered to 16 condom and foley catheters in this review (Fig. 6).

17 Condom catheters are typically used by a male patient who suffers from urinary incontinence. It 18 comprises a sheath, known as the condom, which houses the penis and a tube that connects the tip 19 of the sheath to a collection bag where the urine will be collected. While a condom catheter can be 20 an attractive choice as it is being worn externally, the condom is susceptible to detachment leading 21 to urine leakage. Also, it was reported that 15% of condom catheter users suffered from either 22 necrosis, ulceration, inflammation, gangrene, or constriction of the skin of the penis, and 40% of 23 users developed a urinary tract infection ²¹.

24

The foley catheters comprise two channels, the drainage channel and the inflation channel. The drainage channel is used to drain the urine, while the inflation channel inflates the balloon at the end of the catheter with sterile water. The inflated balloon allows the catheter to be retained within the bladder. Foley catheter can be connected to the bladder by either transurethral or suprapubic catheterisation ²¹. Transurethral catheterisation refers to the insertion of a foley catheter through the natural ureteral passage. In contrast, suprapubic catheterisation refers to creating a track from the bladder to the lower abdominal wall.

32

33 Antimicrobial strategies for urinary catheters are achieved through the use of coatings with 34 antifouling or biocidal properties. The use of antifouling coasting hinders the formation of biofilm 35 by preventing bacteria attachment on the surface. There are three mechanisms of antifouling 36 coating to prevent bacteria attachment on the surface of the urinary catheter. They are electrostatic 37 repulsion, steric repulsion, and low surface energy. Biocidal coatings decrease the deposition in 38 the urinary catheters by killing the microbes. Silver and antibiotics have been identified as active ingredients among the clinically tested biocidal coatings ²⁰. The mechanism of biocidal action can 39 40 be broadly categorised into five categories, as summarised in Table 5.

- 41 2.6 Silicone as Reconstructive Gel Fillers in Plastic Surgery
- 42 The breast reconstruction procedure has been around for more than a century since the first lipoma
- 43 transplant was conducted in 1895²². Since then, various materials have been used as breast fillers,
- 44 including glass balls and uniquely formulated poly (vinyl alcohol). Silicone was first introduced

1 in 1961, where a silicone gel-filled breast implant was developed by Doctors Cronin and Gerow,

2 with materials supplied by Dow Corning. Subsequently, the first pair of silicone gel-filled breast

3 was implanted in 1962. Silicone breast filler was popular for decades, but controversies related to

4 breast cancer, tissue disease, and quality complications lead to rupture, infection, or capsular

5 contracture resulting in FDA restrictions in 1992. In 2006, FDA restrictions were lifted with

6 improved manufacturing practices and the lack of credible causal relationship between breast

7 implants and diseases related to connective tissues 5 .

8 Silicone gel has been used to recover soft tissue mass in the breast, scrotum, chin, nose, cheek,

9 calf, and buttocks via reconstructive plastic surgery. These implants sometimes consist of an outer

shell made of silicone-containing filler made of either silicone gel or saline ⁵. The fundamental

11 properties of silicone that made it such a popular choice as soft tissue replacement are its ideal

13 not spread in order for it to be successfully accepted by the host 23 .

14 One of the most well-known biomedical applications of silicone implants is their use in mammary

15 prosthesis, most known as breast implants. The primary function of breast implants is to enhance

16 the dimensions of the person's breast. There are typically administered to restore the breast's shape

17 for patients who have to undergo mastectomy or correct deformities from congenital disabilities.

18 Besides its use in reconstructive plastic surgery, individuals have also used breast implants for

- 19 aesthetic purposes.
- 20

The primary construct of a silicone breast implant comprises a shell made from Silastic silicone 21 rubber that is filled with soft silicone gel ¹⁴. Silicone's biocompatibility, thermal stability, low 22 23 surface tension, and low chemical reactivity make it suitable for use as a shell for implant¹. First-24 generation silicone breast implants were introduced in 1962 by Cronin and Gerow; since then, 25 significant improvement has been made on the implants' shell and filler material. For example, the 26 shell has been made thicker with three silicone elastomers layers to reduce the gel bleed 27 occurrence. The silicone used in the breast implant filler has also been modified to increase its 28 durability and reliability¹.

29

30 After implantation, the host tissue's immune response would be triggered as it identifies the

31 silicone implant as a foreign object. The initiated immune response results in a collagen fibre

32 capsule to be formed around the surface silicone implant. While the formation of the capsule is a

33 normal tissue response and is relatively harmless, it becomes problematic when the capsule around

34 the silicone implant contracts. The contraction will cause the breast to deform and harden, resulting

35 in a complication known as capsular contracture 24 .

36 Capsular contraction formation can be exacerbated by infection, haematoma, silicone implant 37 leakage, and trauma. Several studies have associated capsular contraction formation with the

38 biofilm formed by *Staphylococcus epidermidis* on the implant's surface. Prevention of initial 39 formation of biofilm is achieved by administering systemic antibiotics or antiseptic washing of the

40 breast cavity to a varying degree of success. In-vitro experiment exploring the application of the

41 antimicrobial coating on breast implants, chloramphenicol, fusidic acid, and oxytetracycline was

42 shown to prevent biofilm formation for a minimum of 7 days 25 .

1 2.7 Craniofacial prosthesis

Silicone is used extensively in the fabrication of craniofacial prostheses such as ear, nose, or eye/eyelids prosthesis. Modern silicone is a suitable material for the fabrication of craniofacial prosthesis as they are flexible and adapts readily to body temperature ²⁶. These silicones can be manipulated to be transparent by restricting the material's thickness, which increases the material's ability to blend into the face seamlessly when applied. In addition, modern silicone can be infused with pigments and hairs to improve the overall aesthetic of the prosthetic ²⁶.

A craniofacial prosthesis is artificially fabricated to replace part of the face that has been lost by trauma, disease, or congenital disabilities ²⁷. It can be both physically and psychologically traumatising for a patient living with facial defects leading to psychosocial dysfunction of the patients ^{26,28}. The use of well-made craniofacial prosthesis can improve the patient's selfconfidence and self-esteem, thereby enhancing their quality of life ^{26,28}.

- 13 Fig. 7 shows an auricular prosthesis and a completed orbital prosthesis, respectively. An auricular
- 14 prosthesis needs to be replaced every 2-3 years because of a change in colour and structure 26 . An
- 15 orbital prosthesis consists of an ocular prosthesis insert, artificial eyelashes, and fixed eyelids ²⁸.
- 16 To reduce the chance of infection of tissues in contact with the silicone prosthesis, regular cleaning
- 17 of the silicone prosthesis using chemical disinfectant is required. Common antimicrobial strategies
- 18 employed involve removing biofilm through toothbrushing or washing by hand with a mild soap $\frac{20}{10}$
- 19 solution 29 .

20 With the advancement of additive manufacturing, direct 3D printing of silicone prosthetics is

- 21 possible. CAD/CAM technology precisely develops prosthesis with soft tissues with 3D printing
- 22 and rapid prototyping ^{30,31}. Fig. 8 illustrates direct 3D printed silicone nose prosthetic and silicone
- ear prosthesis, respectively. It is evident from both figures that the technology is far from ideal and
- 24 requires post-processing, such as surface finishing, to improve the silicone prosthetic aesthetic.
- 25 2.8 Peripheral nerve conduit
- Silicone tube segments can be used as a nerve conduit to assist in nerve regeneration for patients with peripheral nerve gaps ^{32,33}. This treatment is known as tubulisation. It involves enclosing both ends of the severed nerve in a tube ³². In addition to bridging the nerve gap, the usage of the silicone tube segment helps to shield the nerve from surrounding tissues preventing scar formation and helps to guide the regenerating axons to the distal nerve stump ^{32,34} Fig. 9A illustrates the transplantation of the silicone tubing to the severed sciatic nerve of a rat and Fig. 9B shows the regenerated nerve eight weeks after the implant surgery.
- Silicone tubes are soaked in either heparin saline or standard saline solution before used ³². Also, 33 to prevent the formation of blood products and clots in the enclosed area, the conduit's lumen is 34 35 filled with sterile saline water ³². Silicone is a suitable material for synthetic nerve conduits as it is 36 biocompatible and does not break down readily. Its resistance to degradation ensures sufficient 37 time for axons to regenerate, thereby allowing the nerve to regenerate and mature 32 . However, the 38 material also has its drawbacks. Firstly, silicone is nonabsorbable and not biodegradable. It will 39 remain in the body after the nerve has regenerated and will result in the formation of a permanent 40 fibrotic encapsulation around the implant leading to the compression of the newly generated nerve 41 ³². The compression of axons in the silicone implant can lead to the late loss of functional recovery 42 32 . Also, the use of silicone tubing can cause discomfort, as discussed in a study investigating the
 - 8

repair of the forearm median and ulnar nerve using silicone tubing ³³. In a study, seven out of 26
 participants wanted removal of silicone tube due to the irritation caused by the implant and the
 loss of nerve function ^{25, 26}.

4

2.9 First metatarsophalangeal joint implant

5 6

7 This section will discuss the use of silicone implants as a replacement for the first 8 metatarsophalangeal joint. The usage of the first metatarsophalangeal joint implant is an alternative 9 treatment for patients with end-stage arthritis ³⁵. The primary goal of the joint implant is to restore 10 motion and relieve pain to the patient ³⁶.

The use of the silicone implant to replace the first metacarpophalangeal joints was introduced in 12 1967 ³⁶. Before the use of silicone, the uncemented metal metatarsophalangeal joint implant was 13 used in the 1950s ³⁵. These early implants lead to significant complications such as implant 14 loosening, implant instability, and bone resorption ³⁶. Silicone became a favourable choice for the 15 implant as it is biocompatible, has good thermal and chemical stability.

16 In the original iteration of the silicone implant, a single-stem silicone rubber implant was used 17 following a resection arthroplasty to replace the base of the proximal phalanx ³⁶. Subsequently, a 18 constrained double-stemmed silicone elastomer implant with a flexible hinge was introduced. 19 These flexible hinges of the implant were used to replace both the base of the proximal phalanx as 20 well as the head of the first metatarsal. These implants have a high failure rate that is attributed to 21 the wear and tear caused by high shear force and the interaction of the implant with sharp edges of 22 bones ³⁶. Metal grommets were added to reduce the double-stemmed implant's failure rate by 23 creating an interface between the hinge of the implant, and the bones ^{35,36}

The silicone implants act as a dynamic spacer, and it restores the joint user motion while retaining 24 its alignment and joint space ³⁶. However, these implants are susceptible to degradation from 25 ageing, leading to failure. When the silicone implant fails, it will shorten the first ray, leading to a 26 27 cock-up deformity of the hallux ³⁵. The patient will then have to decide to either remove or replace the silicone implant or arthrodesis treatment ³⁵. Besides, the particulate debris from silicone 28 29 implants can cause lymphadenopathy, reactive synovitis, osteolysis, and granulomatous reactions 30 36 . Antimicrobial strategies applied to orthopaedic implant includes the application of antiseptic, antibiotic, antiseptic, photoactive-based, and nano-silver coatings ³⁷. 31

32 **3** Antimicrobial Strategies of Silicone Biomaterial

Antimicrobial strategies use on contact lenses can be broadly categorised as active and passive 33 34 chemical strategies. Active chemical strategies use microbicidal chemicals to eliminate 35 microorganisms by meddling with key microbial cell processes, while passive chemical strategies 36 prevent microorganism adhesion. Examples of active strategies include producing concentrated 37 superoxide toxic to microbial cells or causing cell lysis by physically disrupting the microbial cell 38 membrane. Some of the antimicrobial agents categorised under active chemical strategies include 39 silver, free-radical producing agents, antimicrobial peptides, quorum-sensing blockers (furanone), non-steroidal anti-inflammatory drugs ³⁸— Fig. 10 schematic displaying different explored 40 41 antimicrobial agents to design antimicrobial contact lenses.

1 Passive chemical strategies modify the surface properties to prevent microorganism adhesion and 2 the formation of biofilm. One such example would be the covalent attachment of 2-3 methacryloyloxyethyl phosphorylcholine to the silicone lens. This treatment increases the 4 hydrophilicity of silicone lenses, reducing macrophage's surface adhesion, lens epithelial cell, and platelet. Alginic acid, poly(ethylene glycol) of varying chain lengths, and superhydrophilic 5 6 zwitterionic interfaces are other coatings studied that hinder microorganism adhesion ¹⁷. While 7 being extremely biocompatible, silicones are highly hydrophobic and a significant attraction for 8 bacterial, proteins, and biomolecules adherence, potentially leading to severe infection that might

9 cause death 7 .

10 In most catheter applications, antimicrobial strategies are critical as the catheter exposes the

11 implant location to the atmosphere and invites bacterial adhesion. Ironically, the second most

12 common cause of death to peritoneal dialysis (PD) patients is through the PD catheter, where

13 omental wrapping and infection occurs either through biofouling from protein adsorption and cell

14 adhesion or bacterial attachment ³⁹.

Silicone breast implant augmentations were noted to promote inflammatory responses. Visible 15 16 deformation was noticed around the prosthetic, and over a long term, calcification was observed 17 (fibrous envelope around the implant), leading to pain and skin deformation resulting in removal 18 or replacement of implants. It is worth noting that bacterial contamination from Staphylococcus *epidermidis* at the implant's surface results in excessive fibrotic reaction ³. Various antimicrobial 19 20 strategies are reported to ensure the implant is antimicrobial such as bacteria repelling, bacteria-21 killing, adsorption of proteins or protein conformation, immobilisation of biomolecules - enzymes, 22 peptides, drugs, bioactive polymers, and introduction of inorganic components (SiO₂, TiO₂, ZnO metal) and nanoparticles $3,\overline{40},41$. 23

24 Bacterial contamination of breast implants due to infection and capsular contractures is significant ⁴². The post-operative capsule around the implant is a thin and protective barrier between the 25 foreign material and body that can become pathogenic form called capsular contractures ^{3,42}. 26 27 Surface coatings of implants are pretty standard by immersing the implant with an antiseptic 28 solution (betadine or hydrogen peroxide) before surgery; however, most complex coatings using 29 nanoparticles or antibiotics were recently developed to resist bacterial growth using the 30 bactericidal mechanism. Studies have shown that plasma-activated silicone surfaces offer better 31 coating with antibiotics that inhibited both gram-positive and gram-negative growth ⁴³. 32 Researchers added that plasma activation of silicone implant changes its surface properties from 33 water-repelling to water-absorbing, allowing antibacterial agents to get adsorbed on the implant's 34 surface. Plasma activated silicone discs were treated with 10% povidone, iodine, Cefazolin, or 35 Gentamicin and were exposed to Staphylococcus aureus or Pseudomonas aeruginosa. They added that plasma-activated silicone discs with antibiotics inhibited bacterial growth compared to non-36 37 plasma activated discs ⁴³.

Surface modification techniques have been commonly employed to improve the antibacterial properties of catheters. Anjum et al. presented four major biomodification strategies for urinary catheters: functionalisation, coating, drug impregnation, and blending. The first two results in bacteriostatic surfaces, whereas the latter two results in bactericidal surfaces (Fig. 11) ⁴⁴. Functionalisation can be achieved through gamma, UV or plasma activation, where free radicals are grafted to the functionalised catheter surface, thus adding polymer brushes and bioactive agents, preventing adhesion of bacteria. Silicone catheter surface can also be coated with combinations of antimicrobial agents and antibiotics. The drug impregnation process submerges
 the catheter in antimicrobials, such as chlorhexidine and triclosan, allowing the solvent to swell
 the catheter overtime before drying it and leaving the silicone catheter with a bactericidal surface.

- 4 For blending, a bioactive agent is directly added to the formulation of the catheter material.
- 5 However, it was not discussed if this method is used on silicone catheter 44 .

6 Li et al. noted that hydrophilisation of silicone PD catheter surface is usually temporary, as PDMS 7 can recover the hydrophobic surface within hours by rearranging its polymeric chains. They have 8 also presented a more effective technique through the attachment of hydrophilic functional 9 polymers via covalent bonding, such as PEG polyethylene glycol, which delayed hydrophobic recovery of silicone surface longer than 30 days^{5, 37}. It is important to note that bacterial infection 10 11 of the catheter is still a significant issue in the healthcare industry, and a combination of 12 antibacterial strategies should be employed to maximise the effectiveness of preventing bacterial 13 adhesion. There has also been increasing interest in applying nanomaterials in the delivery of 14 antimicrobial agents, with the promising potential of penetrating the biofilm that has so far been providing a very effective microbial resistance towards conventional antibiotics ⁴⁴. 15

16 **4. Interaction of Silicone Biomaterial with Host Tissue**

17 4.1 Soft Tissue

18 Human soft tissue acts as the host for the silicone soft tissue filler in aesthetic implant and 19 reconstruction. The host's short and long-term response has been researched extensively in cases

20 involving facial scars correction and breast implant 23,45,46 . As with any implants, silicone gel

21 triggers the foreign body reaction, a defence mechanism of the immune system. When the foreign

body is introduced, the immune system will trigger wound healing cells such as macrophages,

causing inflammation or isolation through fibrosis, and eventually, a fibrous capsule will form and

24 surround the implant ⁸.

25 In a microscopic examination conducted by Zappi et al., 35 skin biopsies samples were observed in which liquid injectable silicone [LIS] was administered in 25 patients for face scar correction 26 27 between 1 and 23 years. No significant adverse effect was observed around the silicone droplets that demonstrated inertness and high permanence of silicone ⁴⁵. Authors reported that if LIS is 28 29 used appropriately, it could be a valuable filler for tissue augmentation, especially for treating 30 depressed scars and defects³¹. Christensen reported the clinical observations of gel-host tissue interaction, showing the foreign body reaction and fibrous network around the gel formed by 31 32 macrophages, preventing further migration and fixing its location within the surrounding host 33 tissue ⁴⁶. The literature has sufficiently proven the biocompatibility and permanence of silicone 34 soft tissue filler in the host. However, silicone implants are not without complications. As 35 excessive fibrous connective tissues accumulate around the implant, a strong enough contractile 36 force from the collagen and myofibroblasts may rupture the silicone implant ⁴⁷. Hence, the 37 manufacturing quality of silicone implants needs to be well regulated.

38 4.2 Bone Tissue

39 In the treatment of arthritis, silicone is inserted as a spacer and hinge to replace cartilage and soft

40 tissues between bones. Since the initial development in 1966, silicone implant arthroplasty has

- 41 gone through multiple revisions due to failures relating to wear and fracture of the silicone implant
- 42 48. These failures were initially attributed to tears due to bone spikes, which eventually propagated,

1 leading to structural failure. Later, it was also discovered that ulnar deviation reduces the number

of cycles before failure, as proven by Drayton et al. ⁴⁹. When comparing the mechanical properties,
 bones are a few magnitudes harder than silicones; hence, repeated cycles would eventually result

4 in wearing the silicone implant.

5 4.3 Ocular Tissue

6 The corneal epithelium is the outermost surface of the cornea, which acts as a host to contact 7 lenses. It is constantly renewing to defend against invading pathogens, as well as to provide the 8 refractive surface which is required for vision. The presence of a contact lens triggers an immune 9 reaction known as epithelial homeostasis, which is an inflammatory reaction of the cornea, found 10 to be associated with dryness and lack of oxygen due to extended wear. Silicone hydrogel lenses 11 have been shown to have significantly reduced the response on short-term proliferation, mainly

12 due to its high permeability 50.

13 **5. 3D Printing for Silicone-based Applications**

14 3D printing is an additive manufacturing process that produces a 3D object directly from a CAD

15 model by depositing materials layer by layer⁵¹. Established material deposition methods are either

16 droplet-based, extrusion-based or laser-based. Complex silicone-based materials such as PDMS

17 have been a challenge for 3D printing due to their low elastic modules and support requirement⁵².

Hence, there has not been prominent usage of 3D printing in the biomedical industry using siliconebiomaterials.

Recent advances have seen the emergence of silicone-based printing technologies, which promises the future development of silicone-based bioprinting. 3D printing of PDMS polymer for complex structures is a challenge due to its low elastic modulus. Hinton et al. reported an innovative technique of using hydrophilic Carbopol gel to support the printing of hydrophobic PDMS

technique of using hydrophilic Carbopol gel to support the printing of hydrophobic PDMS prepolymer resins, using freeform reversible embedding (FRE)⁵². Carbopol supports and acts as Bingham plastic, and when the 3D printer syringe moves through the gel and serves as a solid for PDMS. After curing for 72 h while maintaining the dimensional stability, the gel is removed using a phosphate saline solution. The authors reported the use of Sylgard 184 PDMS to print helical

and cylindrical tubes, highlighting the potential of the FRE printing technique for research

- 29 applications. This FRE technology has been adopted by Abdollahi et al. in the printing PDMS
- 30 elastomer cuffs for the wearable pulse oximeter that can be modelled specific to the patient's finger $(F_1 = 12)^{53}$
- 31 (Fig. 12) ⁵³.

20

21

22

It was also interesting to note that a 3D printed PLA (polylactic acid), silicone elastomer-based prosthesis fitted with a leather glove, nylon, and elastic wire was reported. The authors added that patients fitted with 3D printed prosthesis had better hand performance than without aid. The patient performed complex tasks such as opening a plastic bag ⁵⁴. Unkovskiy et al. (2020) reported direct silicone printing of facial prostheses with multi-material silicone with four nozzles ⁵⁵. The auricular prosthesis made of silicone with various grades of flexibility and shore hardness will enable patient's perception of rehabilitation and fitted well with their anatomy.

39 Some of the problems of 3D printing silicone inks with high viscosity are difficulty mixing and

40 changing inks to produce devices and limited to one-part (modulus) or two parts (high viscosity)

41 objects of a single modulus. Recently researchers Zheng et al. (2018) reported the use of rapidly

42 curing low viscosity silicone inks with a single nozzle to produce soft elastomeric materials⁵⁶.

Elastomers of different modulus in different ratios are mixed, and extrusion is delivered by lowpressure devices that are controlled for ink switching and producing multiple objects without causing any dripping during 3D printing. Rapid curing using a UV exposure system (cure <2 seconds and complete cure <20 seconds) avoids the use of support material and offers excellent adhesion between printed layers. Such developments will enable producing complex 3D-printed prosthetic structures with different colours or modulus with rapid prototypes, which enables

7 visualising and identifying the desired fit with the human anatomy.

Along with further advancements in 3D printing techniques, we can expect to see more useful silicone-based bioprinting applications. Coupled with silicone biomaterials' versatility, this should be an exciting development in the field of biomedical. In finger joint implants, 3D printing allows the silicone spacer's complex design to distribute better load catered to each patient's unique condition. Nevertheless, silicone-based bioprinting is still in the early stage, and this application must achieve high standards of quality before it can serve as an implant in the human body.

14 6 Tissue Engineering and Regenerative Medicine Applications

15 Silicone biomaterial has been adopted in regenerative medicine applications. In 2009, Di Girolamo

16 et al. reported the successful use of silicone hydrogel contact lenses to culture. They transferred

17 limbal stem cells to reconstitute the ocular surface of patients with limbal-SC deficiency (LSCD),

18 which is a promising new technique for ocular surface rehabilitation ⁵⁷.

19 Regenerative medicine application towards medical implants is still very much in the conceptual

20 stage. However, it is an area that should be invested in the future development of implants. As

silicone implants today are mostly inserted and isolated in the body, tissue-engineered implant

22 potentially has the capability of being totally and permanently integrated as a part of the body.

23 **7** Outlook of silicone as a biomaterial

The future of silicone biomaterial application will probably lie in its use as a filament material to create prostheses and joint implants. Recent research has shown the possibility of direct 3D printing of silicone facial prosthesis as discussed in section 2.5 and multi-material printing of silicone prosthesis with different flexibility grades ⁵⁵. Despite the progress, these 3D-printed prostheses are far from perfect and require post-processing procedures to achieve a natural aesthetic. Future work in the area could be refining the print resolution to achieve better print texture and the incorporation of complex colouring schemes to produce higher quality prints.

31

For the silicone implant, a recent breakthrough in direct 3D printing of medical-grade silicone meniscus implant opens the door for printing personalise silicone implants ⁵⁸. Despite the progress, the printing technology will likely be restricted to printing purely silicone parts or implants instead of multi-material print such as the double-stem silicone first metatarsophalangeal joint implant with a metal grommet. Incorporating a different material introduces a second set of settings that will likely differ from the ideal setting required for successful direct printing of silicone whose

38 quality is susceptible to variables such as the nozzle diameter, platform temperature, nozzle

39 temperature, and material flow rate ⁵⁸.

40 It is worth noting that silicone's future as a biomaterial depends on its ability to demonstrate 41 antimicrobial properties, particularly for applications including mammary prosthesis, contact lenses, and urinary catheters. The application of silicone for peripheral nerve regeneration will likely be phase out in favour of a 3D bio conduit in the future. Bio conduit offers a safer alternative to silicone conduit as it is composed of pure biological tissues. Thus patients who undergo bio conduit transplantation will likely have a lower chance of infections, allergies, and foreign-body reaction than patients with silicone conduit transplantation ³⁴. Furthermore, bio conduit yields significantly better results compared to silicone conduit in terms of the wet muscle weight,

7 morphology, electrophysiology, and kinematics of the regenerated nerve ³⁴.

8 8 Conclusions

9 From work presented here, it can be concluded that silicone has found application in the biomedical

10 industry due to its chemical stability, excellent mechanical properties, biocompatibility, and bio

11 durable when interacting with host tissues. Silicone polymers are versatile and can be formulated

12 into various distinct material types, including elastomers, gels, adhesives, fillers, and more,

13 depending on the desired application. Silicone elastomers are used in medical devices, whilst

silicone gel for treating hypertrophic burn scars. Besides being thermally stable, it allows for sterilisation using steam or gamma radiation, making them suitable for therapeutic applications.

16

17 In this review, eight different applications [medical inserts, speciality contact lens, drains and 18 shunts, urinary catheter, reconstructive gel fillers, craniofacial prosthesis, nerve conduit, and 19 metatarsophalangeal joint implants] were critically discussed to highlight the expansiveness of the 20 healthcare applications. These applications that use silicone polymers are highlighted, indicating 21 the field's development and the specific changes required to suit the intended application and 22 challenges incurred when using silicone in different forms. The timeline also reiterates that 23 silicone's application as biomaterial commenced way back in the 1950s as implants or coating 24 syringes that significantly reduced pain due to less insertion force and early 1960s for breast 25 implants that created enormous attention in reconstructive plastic surgery. Silicone tubing used as 26 biomedical devices also highlights silicone's stability, hemocompatibility, and high oxygen 27 permeability when serving to transport body fluids.

28

29 One of the significant developments in using silicone hydrogels as a contact lens is where 30 continuous wear was reported with no infection replacing the disposal hydrogel lenses. These were 31 possible due to their high oxygen permeability and low chemical reactivity. It is also worth noting 32 the silicone gel fillers and their reconstructive plastic surgery application, mainly in breast 33 implants. Capsule formation around the silicone implant and later its contraction was resulting in 34 infection, leakage, and trauma. There were concerns due to the implant being susceptible to 35 bacterial infection - various aspects of enabling silicone polymer resistance to microbial infection with antibiotics were critically presented. These include surface coating, modification or 36 37 impregnating with antibiotics, adsorption of proteins or protein conformation, immobilisation of 38 biomolecules - enzymes, peptides, drugs, bioactive polymers, and introduction of inorganic 39 components (SiO₂, TiO₂, metal) and nanoparticles.

40

41 One of the silicone's fundamental properties as the first choice for soft tissue replacement is its

42 texture and stability. Recent developments enabled manipulating silicone properties, being flexible

43 in various thicknesses, and blended with the human anatomy for use as craniofacial prosthesis -

44 ear, nose, and eye/eyelids. Additive manufacturing enabled 3D printing of silicone inks of low

45 viscosity with varying modulus to produce complex structures and allow rapid prototyping. Future

1 work would aim to refine the print resolution to achieve better texture and incorporate complex 2 colouring schemes to produce higher quality prints. Also, direct 3D printing of medical-grade

- 3 silicone meniscus implants opens the opportunity for printing personalised silicone implants.
- 4

5 It is worth noting that silicone's future as a biomaterial depends on its ability to demonstrate 6 antimicrobial properties, particularly for applications including mammary prosthesis, contact 7 lenses, and urinary catheters. These could be surface coatings with nanoparticles or treated with 8 antibiotics or plasma-activated silicone implants treated with antibiotics to resist bacterial growth. 9 Surface modification techniques using functionalisation are achieved by gamma and UV treatment 10 where free radicals are grafted to the surface, thus adding polymer brushes and bioactive agents to prevent bacterial growth. It is also noteworthy to highlight silicone biomaterial interactions with 11 host tissue (soft tissue, bone tissue, and ocular tissue) and their unique ability to be inert, 12 13 chemically stable, and high permanence. Silicone-based biomaterials' future remains bright if the 14 device manufacturers maintain their responsibility to appropriately screen and source their raw materials. Besides, with the emergence of silicone-based 3D bioprinting and tissue engineering 15 16 technologies, silicone has a large part to play in the medical industry's future. Besides, it remains a challenge to ensure the implants are safe, biocompatible; the material is high quality and well-17 regulated to avoid adverse reactions. In this review, the critical properties of silicone are 18 19 highlighted for biomedical uses showing its versatility and how it can be used in varied formats to 20 suit different applications. It is essential to note that the application's specific requirements should be thoroughly studied before selecting and designing an optimal silicone to meet their needs. 21

22

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15 **Figure Captions**

- 16 Fig. 1 Schematic synthesis of silicone, R₁=R₂=CH₃-Polydimethylsiloxane (PDMS), R₁=CH₃, R₂=Phenyl-
- 17 Polydimethylsiloxane, $R_1=R_2=$ Phenyl- Polydimethylsiloxane, $R_1=CH_3$, $R_2=$ Fluoro, polyether, other functional 18 groups
- 19 Fig. 2 Key milestones in the development of silicone chemistry
- Fig. 3 A) Penetration force of silicone coated and noncoated hypodermic needles, as measured by B) Melab
 equipment
- Fig. 4 X-ray view of a right hand with arthritis before (left) and after (right) restorative implant surgery
- Fig. 5 Holter shunt use for treatment of hydrocephalus
- 24 Fig. 6 A) Condom catheters B) Foley catheters
- Fig. 7 A) Image of a patient with auricular deformity B) Image of a patient with an auricular prosthesis. The Image of a completed orbital prosthesis with coloration applied. A) Front view B) Sagittal view C) Posterior view
- 27 Fig. 8 Image of direct 3D printed silicone ear prosthesis. A) Print without post-processing B) Print ground with
- 28 polishing paper C) Polish print with silicone material seal in areas unreachable by polishing tools D) Coloured
- 29 polished print. The Image of direct 3D printed silicone nose prosthesis. E) Print without post-processing F) Print
- 30 that has been coloured and sealed with silicone coating G) Print that has been coloured, sealed with a silicone
- 31 coating, and polished with a fine milling cutter
- Fig. 9 A) Image of the transplantation of a silicone tube to the sciatic nerve defect model of a rat. B) Image of the regenerated nerve 8 weeks after surgery
- 34 Fig. 10 Schematic representation of bacterial activity on bacteriostatic and bactericidal surfaces
- 35 Fig. 11 Schematic revealing different chemical strategies to design antimicrobial contact lenses

1 Fig. 12 - Printed PDMS elastomer cuffs tailored to a specific patient and integrated into a wearable pulse oximeter

2 Table Captions

- 3 Table 1 Properties of silicone and other common soft polymers
- 4 Table 2 Examples of silicone implant in human body
- 5 Table 3 Characteristics of conventional hydrogel and silicone hydrogel contact lens.
- 6 Table 4 Catheter materials and comparison
- 7 Table 5 Summary of 5 of the most common biocidal mechanism in the biocidal coating.
- 8



9

- 10 Fig. 1 Schematic synthesis of silicone², $R_1=R_2=CH_3$ -Polydimethylsiloxane (PDMS), $R_1=CH_3$,
- 11 R_2 =Phenyl- Polydimethylsiloxane, R_1 = R_2 = Phenyl- Polydimethylsiloxane, R_1 = CH_3 , R_2 = Fluoro,
- 12 polyether, other functional groups





ssful synthesis of first silicone organic Succ compound -tetraethylsilane $2\text{Zn}\,(\text{C}_2\text{H}_5)_2 + \text{SiCl}_4 \rightarrow \text{Si}(\text{C}_2\text{H}_5)4 + 2\text{ZnCl}_2$

Frederic Kipling develops various silane preparation methods and helping to establish the study of organosilicone chemistry

First published record of silicone elastomer

implant in humans for bile duct repair

1863

1901-1930



SILICONE CHEMISTRY

potassium; 4K+K₂Si F₆ → Si +6KF Formation of tetrachlorosilane by reacting with silicone with chlorine; $Si + 2Cl_2 \rightarrow Si Cl_4$

1871 Observation of diethyldiethoxysilane (C2H3) 2Si (OC₂H₅)₂ in diluted acid

1940

1948

from silicone

1962

1979

approved by FDA

2008

technique

James Franklin Hyde of Dow Corning demonstrated the high electrical resistance and thermal stability of silicone resins. Eugene George Rochow of General electric discovery of silicone preparation directly from methylchloride and silicone observation of diethyldiethoxysilane



1949

1946

Prevalent use of silicone precoating in blood collection vials, syringes, and needles after researchers at Mayo clinic demonstrated that there is no significant effect on blood left in the silicone-coated syringe

1969 Introduction of posterior offset hinged total knee implant with silicone bumper incorporated for shock absorption

1999 Launch of silicone hydrogel contact lenses



2010 onwards

3D printing and antimicrobial strategies using various surface modifications

Development of silicone





Implantation of the first pair of silicone gel breast implants in a woma



Application of silicone as biomaterial

The Anglechik antireflux prosthesis use of

gastro-esophageal reflux management became first device with silicone gel that is

Silicone biodurability after long term implantation was examined by highly sensitive NMR spectroscopy



Fig. 3 (A) Penetration force of silicone coated and noncoated hypodermic needles, as measured by (B) Melab equipment using DIN 13097



Fig. 4 X-ray view of a right hand with arthritis before (left) and after (right) restorative implant surgery ⁵





polishing paper C) Polish print with silicone material seal in areas unreachable by polishing tools D) Coloured polished print ⁵⁵. The Image of direct 3D printed silicone nose prosthesis. E) Print without post-processing F) Print that has been coloured and sealed with silicone coating G) Print that has been coloured, sealed with a silicone coating, and

polished with a fine milling cutter ⁶¹



- Fig. 9 A) Image of the transplantation of a silicone tube to the sciatic nerve defect model of a rat. B) Image of the regenerated nerve 8 weeks after surgery ³⁴.



Fig. 10 Schematic revealing different chemical strategies to design antimicrobial contact lenses.



Fig. 11 Schematic representation of bacterial activity on bacteriostatic and bactericidal surfaces ⁴⁴



9 Fig. 12 Printed PDMS elastomer cuffs tailored to specific patient and integrated into a wearable pulse oximeter ⁵³

1 Tables

2 Table 3 Properties of silicone and other common soft polymers ^{2,8}

Polymer	Tensile strength (Mpa)	Elongation (%)	Tg (°C)	Tm (°C)	Water absorption (%)	Water contact angle (°C)	Biomedical applications
Polydimethylsiloxane (PDMS) or silicone	2-10	100-600	120- 123	-	0.02	101- 109	Oxygenator membrane, tubing, Shunts, prostheses, heart peacemaker leads, heart valve structures, burn dressing
Silicone Elastomers	8-10	300-800	-130	-	< 0.03		Wound dressing
Low density polyethylene (LDPE)	4-16	90-800	-20	95- 115	<0.01	93-95	Tubing, shunts, catheters
High density polyethylene (LDPE)	21-38	20-1000	-125	135- 138	<0.01	91	Plastic surgery implants, catheters
Polypropylene (PP)	30-38	200-700	-12	125- 167	<0.01	104	Heart valve structure, oxygenator and plasmapheresis membranes, finger joint prosthesis

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1 Table 4 Examples of silicone implant in human body ^{5,8,62}

Location	Rody parts	Annlications		
	Douy parts			
Head and neck	Brain	Hydrocephalus shunts		
	Skull	Burr hole covers		
	Eye	Scleral bands and buckles		
		Vitreous fluid replacement		
		Intraocular lenses		
		Contact lenses		
	Ear	Elastomer tubes for ontological ventilation		
		Cochlear implants (encase in silicone)		
	Throat	Voicebox prothesis, post- laryngectomy		
Torso	Cardiac	Peacemaker encapsulated and leads insulated with silicone		
		Mechanical heart valves		
	Gastric	Gastric band implant (Lap-Band, Realise)		
Urinary system	Urinary tract	Silicone urological catheters		
		Urethral stents		
		Artificial urethra		
Skeletal joints	Hip	Silicone drainage systems		
	Knee	Shock-absorbing silicone bumper for knee replacement		
	Foot	Foot and toe joint implants		
Other	Breast	Breast implant for post-mastectomy reconstruction or aesthetic		
		augmentation		
	Scrotum	Testicular implants for congenital defects or post-orchiectomy surgery		
		Bio-scaffolds: 3D porous, cellular therapies used to treat Type I diabetes.		
	Cell therapies	formed by solvent casting and particulate leaching or free form rapid		
	r****	prototyping: PDMS is surface treated to enhance hydrophilicity and cell		
		attachment		

3 Table 3 Characteristics of conventional hydrogel and silicone hydrogel contact lens ^{12,63}.

Material	Silicone Hydrogel	Conventional Hydrogel
Monomers	DMA, siloxane macromer,	MA, HEMA
Initial modulus (MPa)	1.4	0.35
Oxygen permeability	175×10^{-11}	28 ×10 ⁻¹¹
Oxygen transmissibility	175×10^{-9}	31×10^{-9}
Water content	24%	58%
Limitations	Requires hydrophilic monomer, can be abrasive	Protein deposition issues, low oxygen permeability, low water contents,
Advantages	Durable, comfortable	Flexible, inexpensive

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1 Table 4 Catheter materials and comparison ^{19,64–66}

Type of catheter	Maximum time <i>in-situ</i>	Special features
Polytetrafluoroethylene (PTFE) (Teflon) coated latex	28 days	
Hydrogel-coated latex Hydrogel-coated silicone	12 days 12 days	Hydrogel; smooth, compatible with body tissue
Silicone-elastomer coated latex	28 days	Silicone; inert but more rigid
Silver alloy-hydrogel with latex core	28 days	Antibacterial properties
Silicone, hydrogel-coated; phosphate silver ions in coating	12 weeks antimicrobial properties ≤30 days	Antibacterial properties
100% silicone	12 weeks	Thin-walled, large lumen. More rigid than silicone-coated catheters. The surface is less smooth, offers excellent balloon 'cuffing' (unevenness) on deflation of the balloon
HydroSil gripper - hydrophilic silicone -		Intermittent catheters for self-catheterisation – for those
male HydroSil Rose for female		suffering from urinary retention

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3 Table 5 Summary of the most common biocidal mechanism in the biocidal coating 20 .

Inhibition of cell wall synthesisThe presence of biocide hinders dephosphorylation and peptidoglycan phospholipid carrier in peptidoglycans formationPenicillin, chlorhexidine, and vancomycinInhibition of protein synthesisBiocides attachment to the ribosomal subunits in bacteriaNitric oxide, silver ions, and minocyclineInhibition of nucleic acid synthesisBiocides hinder mRNA DNA gyrase, nucleic acid, and topoisomerases synthesis.Nitric oxide, silver ions, and minocyclineEffects on cell membrane sterolsBiocides alter the cell membrane sterols. This mechanism can cause cytotoxicity and is typically used as the final barrier against bacteria.Antimicrobial peptides, triclosan, silver ions, and antifungal agents (amphotericin)Inhibition of unique metabolic stepsBiocides agent can either remain on the surface and eliminate microbes on contact or be released to eliminate the bacteria.Nitrofuran, triclosan, sulphonamide, and bacteriophages	Mechanism of action	Description of action	Examples of agents
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