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Antimicrobial Polymeric Wafers for Diabetic Wound Healing: A Comparative Review of Polymer Composition, Porosity, Drug Delivery and Therapeutic Function

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ABSTRACT:

Diabetic foot ulcers are chronic wounds where high blood sugar, bacterial infection poor blood vessel growth and long-lasting inflammation together slow healing [1–3]. The literature shows that antimicrobial drug-loaded polymeric wafers are porous freeze-dried and can soak up wound fluid while giving medicine right to the wound [4,5]. This review looks at the polymeric wafer systems and related hydrogel, nanofibre and nanocomposite platforms in the source focusing on polymer type, porosity, crosslinking, drying method, antimicrobial approach and how drug is released. Calcium alginate, sodium alginate–gelatin, HPMC/ethyl cellulose/PVP, xanthan gum, CMC, chitosan, carrageenan, pectin and PLGA wafers show that the way the wafer is made controls how it hydrates and how drug comes out [10,11,16–26]. Antimicrobial strategies go from antibiotics to antimicrobial peptides, metal ions and systems that respond to the wound environment [1–6,15]. Often multifunctional wafers bring together antimicrobial, antioxidant, anti-inflammatory and pro-angiogenic actions [7,9,12–15]. Even though preclinical data look good moving wafers to clinic needs checks of stability, safety, biocompatibility and real-world effectiveness.

KEYWORDS

Diabetic foot ulcer; antimicrobial wafer; polymeric wafer; lyophilization; calcium alginate; HPMC; chitosan; controlled release; biofilm; wound healing.

1. Introduction

Diabetic foot ulcers happen in people with diabetes and are a main reason for lower-leg amputation that is not caused by injury. The document says that healing slows because of blood sugar, bacterial infection poor blood vessel growth and long-lasting inflammation [1–3]. Oral or IV antibiotics often do not reach drug in chronic wounds especially when bacterial biofilms are present and they can also create resistant bacteria and upset normal bacteria [1,5]. Giving drug directly to the wound over time is therefore appealing because it keeps medicine at the wound while keeping the rest of the body safe [1,5].

Polymeric wafers are structures that can be made by freeze-drying or similar techniques. Their design lets wound fluid enter and gases pass through. When the wafer takes in water it turns

into a gel-like material that keeps the moist and can be removed with little pain [4,5,10]. A wafer can hold than one medicine so it can combine antimicrobial action with tissue repair [4].

2. Pathophysiology and Rationale for Local Therapy

In a wound high blood sugar, weak blood flow and broken immune responses make it easy for bacteria to grow and form biofilms [6,7]. Chronic inflammation stops skin from forming blocks new tissue build-up and hinders collagen creation [7–9]. Biofilms can resist antibiotic treatment and keep inflammation going [6]. These problems support the idea of giving medicine to the wound so that it works for a long time and can also add more healing help.

3. Wafer Architecture and Drug Delivery

Freeze-dried wafers have open structures that can soak up wound fluid while keeping the wound



moist [4,5]. The paper shows porosity high as about 98% for some wafers and high porosity helps fluid enter and gases leave [19]. Compared with solvent-cast films freeze-dried wafers take in water faster and usually give medicine out faster [16,17]. Therefore porosity helps wound care. It is also a key factor that must be managed to stop a sudden large burst of medicine.

4. Antimicrobial and Bioactive Wafer Systems

A wafer made from calcium alginate and carrying ciprofloxacin released medicine quickly at first and then slowly and it kept skin cells alive well [4]. A wafer made from HPMC, ethyl cellulose and PVP that held curcumin released medicine steadily. Fought bacteria [11]. A calcium alginate–gelatin wafer with linezolid released 96.9% of the drug in 24 hours. Caused no harm in the animal test [5]. A sodium alginate–gelatin wafer that had diosmin nanocrystals released medicine steadily for 8 hours and helped skin grow back fully in mice that had just a sugar spike while a xanthan gum wafer with silymarin helped cells that move blood vessels overcome the bad effect of high sugar [10]. These data show that calcium alginate works for local antibiotic delivery gelatin-based wafers widen the polymer mix and HPMC/EC/PVP works for curcumin that does not mix with water [4,5,11]. Xanthan gum and diosmin/silymarin wafers show a shift from killing bacteria to also helping blood vessels and tissue repair [10].

5. Antimicrobial Agents and Therapeutic Mechanisms

The systems studied use antibiotics, antimicrobial peptides and metal-based or stimulus-responsive medicines. A calcium alginate wafer with ciprofloxacin fought *E. Coli*, *S. Aureus* and *P. Aeruginosa* first giving medicine fast and slowly [10]. A hydrogel that carried both rifampicin and vancomycin helped biofilms by using two different ways to kill bacteria [6]. An alginate hydrogel with human lowered MRSA and also helped new skin grow, remodel tissue and form new blood vessels [3]. Stimulus-responsive wafers use signals from the wound to decide when to give medicine. A

system that reacts to glucose can release zinc ions when there is too much sugar giving antibacterial and blood-vessel growth benefits [2]. A system that reacts to both pH and glucose made of acid and gallium lowered bacterial life and stopped biofilms in wounds that are typical of infected diabetic wounds [1]. A supramolecular wafer that uses linkers that break when proteases or reactive oxygen species are present was made to release peptides when infection signals appear [15].

6. Multifunctionality and Tissue Regeneration

Bacteria is one part of the trouble in diabetic wounds. Good dressings might need to fight bacteria reduce inflammation fight radicals and help blood vessels grow [13,14]. A wafer that carries curcumin and metformin was made to give metformin and curcumin slowly and it helped remove free radicals grow new skin build tissue add collagen and grow blood vessels [7]. A wafer that carries dihydromyricetin gave a step-by-step fight against bacteria, free radicals and inflammation. It also changed macrophage behaviour [14]. A chitosan wafer that had acid and tiny chlorhexidine particles worked well against bacteria stopped free radicals and showed signs of antioxidant defence and blood-vessel growth [12]. A wafer made from acid and chitosan that held curcumin and EGF was made so that medicine comes out at the right time during the wound-healing cycle [9].

7. Polymer Composition and Drug Release Kinetics

Sodium carboxymethylcellulose (CMC) is a wafer polymer that many studies look at. When CMC level goes up the drug comes out slower: the time for half the drug to leave went from 11 minutes with 0.5% CMC to about 175 minutes with 3.0% CMC [16,17]. HPMC can be mixed in ways and can give fast or slow release depending on the type and mix of polymers [11,25]. A wafer made from HPMC, ethyl cellulose and PVP that had curcumin released 23–39% of the drug in 8 hours and when the wafer carried drug the release was less because the hydrophobic drug blocked pores in the wafer [11]. A chitosan wafer released drug than a chitosan film and



stuck to mucus better [26]. A κ -carrageenan/Pluronic F127 wafer, a cross-linked pectin wafer and a PLGA wafer each have their release patterns.

8. Porosity, Crosslinking and Microstructure

Crosslinking is a way to stop a sudden burst of drug. In a pectin wafer adding divalent cations made pores smaller. Made the release slower and steadier [24]. Crosslinking after freeze-drying gave the control in the study with about 40% of the drug released in 30 minutes versus 82% from a wafer that was not crosslinked [24]. When chitosan and alginate linked together the spaces inside the wafer. The wafer swelled less so the burst of drug was smaller [29].

9. Freeze-Drying and Drying Method

Freeze-drying makes a structure and is key to how a wafer works. Freeze-dried wafers take in water faster. Give medicine out faster than thick films [16,17]. Therefore, how the wafer is dried is an important design choice, not just a manufacturing step. Freeze-dried cellulose had about 92% porosity while oven-dried material had about 75% porosity; the freeze-dried version let medicine burst out and the oven-dried version gave a steadier flow [32]. Heating a wafer while freeze-drying, called annealing made a chitosan wafer release BSA in 7 hours by changing how it takes up water and by changing its tiny structure [33].

10. Drug Properties and Release Mechanisms

How a drug behaves chemically interacts a lot with how a wafer's built. Water-friendly drugs usually come out fast at first while water-unfriendly drugs may come out slower and stay longer because they like the parts of the wafer [35]. A drug that is in crystal form may leave the wafer slower than a drug that is all mixed in at a level [35]. A mathematical model called Korsmeyer–Peppas is often used to describe how wafers release medicine [16,17,23,37]. In some cases, a curcumin wafer made from HPMC and a paracetamol wafer made from carrageenan let medicine move by diffusion while ibuprofen, in a carrageenan wafer

showed a mix of diffusion and wafer wearing away [11,23].

11. Comparative Perspective: Wafers, Hydrogels and Nanofibres

Polymeric wafers offer porosity, exudate absorption and localized controlled delivery. Hydrogels provide water content and adaptable responsive chemistry. Nanofibres offer high surface area and tissue

12. Translational Challenges and Future Directions

Emerging systems now include the ability to respond to pH and glucose use heat from light to fight microbes and deliver drugs in a loop [1,13]. Hydrogel systems that react to near-infrared light contain EGF and MXene nanosheets mix heat-based killing with steady release of growth factors [13]. Other systems that respond to glucose make oxygen. Release antimicrobial agents only when needed [13].

13. Conclusion

Antimicrobial polymeric wafers are a promising local treatment for diabetic wounds, according to the publications reviewed. Research using calcium alginate, sodium alginate-gelatin HPMC-based, CMC, chitosan, pectin, and other polymer blends demonstrate that the drug's release is determined by the polymer mix's porosity, cross-linking, and drying methods. Antimicrobial agents can be administered as metal-ion systems, peptides, antibiotics, or natural active chemicals; related hydrogels and nanocomposites advance the concept into responsive and multifunctional therapy.

The most notable comparison is that the drug does not shoot out instantly and stays longer when the structure is closely regulated; on the other hand, when the material is more porous and less firmly cross-linked, it absorbs water more quickly and releases the drug more quickly. The objective of treatment is to switch from a single antimicrobial medication to a regimen that addresses infection, guards against oxidation, reduces inflammation, and promotes the creation of new blood vessels. The majority of research is still in the lab stage, and we require regular



testing, long-term stability checks, comprehensive safety reviews, and carefully thought-out human trials.

Table number 1: Comparative Formulation Table

Formulation	Polymer matrix	Agent	Principal finding	Ref.
Calcium alginate wafer	Calcium alginate	Ciprofloxacin	Initial rapid then sustained release; >85% keratinocyte viability	[4]
HPMC/EC/PVP wafer	HPMC + ethyl cellulose + PVP K-30	Curcumin	Sustained release and antibacterial activity	[11]
Calcium alginate–gelatin wafer	Calcium alginate + gelatin	Linezolid	96.9% release at 24 h; no adverse animal findings	[5]
Sodium alginate–gelatin wafer	Sodium alginate + gelatin	Diosmin nanocrystals	Sustained release over 8 h; complete re-epithelialization in STZ mice	[10]
Xanthan gum wafer	Xanthan gum	Silymarin	Counteracted high-glucose-associated reduction in endothelial migration	[10]

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