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Development of an Optimal Wound Sealing Strategy by Screening Natural and Synthetic Biomaterials

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Abstract: The body can heal itself naturally, but often treatable injuries become fatal due to the delay of treatment. According to the US Army Institute of Surgical Research, hemorrhage from major trauma was the predominant mechanism of soldier death in 80% of potentially survivable trauma.[1] The development of a wound sealer would decrease patient mortality. In developing countries, like India, seventy percent of hemorrhagic shock caused by traffic accident mortalities can be avoided by the availability and optimization of medicinal supplies and proper diagnosis and treatment. [2]

The aim is to study various types of wounds and identify different strategies for making the best suitable wound sealing agent in order to create an instant hemostat or barrier, repair acute tissue injuries, and facilitate long term repairing of surface wounds by improving healing time. A variety of wounds, natural physiopathology, and assisted healing techniques have been studied. A plethora of biomaterials and antibiotics of biological and synthetic origin have been scrutinized based on their biological and physicochemical properties suitable for wound sealing. Lastly, a suitable delivery device has been chosen. A combination of alginate, chitosan, collagen, curcumin, and gentamicin put inside of a glass spray bottle has been decided on.

Introduction: Before designing a wound sealer, many factors must be taken into consideration. Such as identifying types of wounds that can benefit from a biomaterial solution. Certain parameters are set such as the wound must be on the surface of the body and at most 15 centimeters wide. The mechanism of trauma begins with energy being transferred to the body through an outer force. This is known as kinetic energy which can be transferred in a blunt or sharp manner. The third possible mechanism of trauma is thermal energy which can be imparted to the body through heat, cold or a chemical agent which creates an exothermic or endothermic reaction.[3] Wounds are any outside or inside breakage to the tissues of the body. Wounds can be categorized, contingent upon the number of skin layers and on the zone of the skin influenced, as superficial, partial thickness, and full-thickness wounds. Wounds can also be acute or chronic, depending on healing time. They mostly stem from skin conditions, underlying diseases, surgeries, and accidents. Certain groups of people are at a higher risk of complications such as diabetics, cancer patients, pregnant women, elderly, children, obese, and drug abusers.[3][4]

Hemostatic dressings that are already on the market such as Hemospray are not easily portable, inexpensive, or easy to use. WoundSeal Powder is inexpensive and stops bleeding quickly but it is not bioresorbable and must be completely removed for definitive recovery. It causes further damage during removal. QuikClot hemostatic gauze works quickly and can be removed by hydration, but it is expensive, nonbiodegradable, and can cause injury due to an exothermic reaction with the wound.[5] Therefore, there is an utmost need for a hemostatic dressing that can delay excess trauma by retaining fluids, delivering drugs, mitigating blood flow, and healing wounds faster than the body can naturally.[6] It should be nonimmunogenic, anti-inflammatory, biocompatible, portable, inexpensive, easy to fabricate, and stable under adverse weather conditions.

Materials and Methods: This wound sealing spray will create a sealed wound environment to keep out infection while creating moist conditions to promote wound healing.[6] The aim is to make a product that will be able to treat a wide range of injuries from wounds to burns. The spray will be applied to the injured tissue and it will absorb the exudates. The material will become thicker and it will cover and seal the wound, therefore creating a plug that will halt blood flow, effectively sealing the wound. It's antibacterial properties will aid in wound healing as well. Using a biomaterial is beneficial because it can be placed on the skin and it will repair missing tissue and interact with the biological systems. To add another layer of protection either a synthetic or biological antibiotic will be used.

Different formulations of alginate, collagen, chitosan, and polycaprolactone (PCL) will be studied. Such as alginate-collagen, alginate-chitosan, alginate-PCL, collagen- chitosan, collagen- PCL, chitosan- PCL, alginate-collagen-chitosan, and so on and so forth. Next, the best performing combinations will be mixed with gentamicin and curcumin alternatively to see which is the superior antibiotic agent.

Results and Discussion: Evaluation of Biomaterial Based on Salient Properties

The following four biomaterials were chosen based on their properties; Alginate for keeping the wound moist, collagen for wound healing, chitosan for an inflammatory environment beneficial for healing, and polycaprolactone for mimicking the extracellular matrix.[7]

Evaluation of Wound Healing Agents Based on Salient Properties

	Bio-compatibility	Immuno-genicity	Inflamm-atory	Wound Healing	Haemostatic Ability	Drug Delivery	Water Retention	Drawbacks	Used In
Alginate	Yes, bioactive	No	No	keeps wound moist	Proficient, Best with Zinc	Possible thru porosity, Pectin inc delivery	Absorb extra fluid	Impurities can cause immunogenic response	exudating wounds: infected post-op wounds, leg ulcers
Collagen	Yes, bioactive	Weak antigenicity	No	wound contraction, granulation tissue formation, angiogenesis	Proficient, Better than Cellulose	Ciproflaxin mediates wound closure	in sponge form	weak antigenic properties	open, dry wounds
Chitosan	Yes, Biodegradable	immuno-stimulatory activity	Yes	create inflammatory microenvironment for healing	Proficient, Superior to Plain Gauze	safe & effective	N-Succinyl type	Unstable, low mechanical resistance	femoral wounds
Polycapro-lactone (PCL)	Yes, biodegradable, bioresorbable	No	No	mimics ECM with Collagen	Proficient, best with gelatin	PCL & PEG used for drug delivery	absorbs extra fluid	poor antimicrobial properties, needs silver nanoparticles, bad mechanical properties	acute & chronic wounds

Table 1. Evaluation of Biomaterial Based on Salient Properties

The following two wound healing agents were chosen based on their properties; Gentamicin since it's a broad range antibiotic and curcumin because of it's antimicrobial and wound restoration properties.[6][8]

	Advantages	Disadvantages
Gentamicin	broad spectrum, shortens wound healing duration(collagen sponge), controls bacterial growth, improves post op outcomes	mostly ineffective against anaerobic bacteria, fungi and viruses, can't be absorbed thru intact skin
Ciprofloxacin	effective against skin, skin structure infections, active against many Gram negative/positive bacteria, no cross resistance with other classes of antibiotics	Can only be indicated in infections caused by certain susceptible bacteria
Bacitracin	bacteriostatic, bactericidal, works well with gram positive bacteria, burned & granulated skin	gram negative bacteria are resistant, only for minor skin injuries, common allergen
Diferuloyl Methane (Curcumin)	anti-(microbial, coagulant, inflammatory), accelerates wound restoration by stimulating production of growth factors, enhance granulation tissue formation, collagen deposition, tissue remodeling and wound contraction, stimulatory at low doses, topical application better than oral	inhibitory at higher doses, hydrophobic nature significantly limits its application, works on acute wounds

Table 2. Evaluation of Wound Healing Agents Based on Salient Properties

Evaluation of Therapeutic Wound Sealer Delivery Device Based on Salient Properties

A 3ml glass spray bottle has been chosen due to its even application, simplicity, portability, availability, price, size, and nonreactivity.[9]

	Even Application	Ease of Use	Aseptic	Portable	Availability	Price	Reactivity	Size	Flexible	Hemostatic Ability	Water Retention
Aerosol Can	Yes, even spray of biomaterial	Simple	Yes	Yes	Common	Expensive due to filling techniques	Closed Al/Sn/ plastic+ steel environment	5ml volume	N/A	N/A	N/A
Spray Bottle	Yes, even spray of biomaterial	Simple	Yes	Yes, but fragile	Common	Affordable	Closed glass environment	3ml volume	N/A	N/A	N/A
Gauze	Yes, equal distribution of biomaterial	Simple	Yes	Yes	Uncommon, electrospinning facility	Expensive, extra step impregnation	Nonreactive	5cm larger than wound on all sides	Highly	Proficient coverage of wound	soakage of exudates
Foam	Yes, equal distribution of biomaterial	Simple	Yes	Yes	Uncommon	Expensive, due to multiple layers created	Nonreactive	5cm larger than wound on all sides	Highly	Proficient coverage of wound	soakage of exudates many times weight

Table 3. Evaluation of Therapeutic Wound Sealer Delivery Device Based on Salient Properties

Glass Slide and Duran Bottle Experimentation Strategy

Glass slides and Duran bottles were chosen for preliminary testing because they are easy to procure. They are available in large sets that are identical, therefore removing some bias from the experiment. Their shape is advantageous in assessing a variety of qualities of the therapeutic wound sealer fluid such as viscosity, quick drying time, brittleness, flexibility, and adhesiveness.[9]

Skin Organoid Experimentation Strategy

Recently a skin organoid has been developed from human induced pluripotent stem cells. It is equipped with dermis, epidermis, fat cells, hair follicles, sebaceous glands, and nerve cells allowing researchers to explore the function of mixed nerves in the healing of wounds. This could replace half of the in vivo experiments and decrease the number of animal models utilized in studies.[10][11]

Conclusion : Hemostatic agents have a major role in the control of hemorrhage and will diminish related mortality and death. Currently, there is no sole hemostatic agent that will work eminently better than others in varied conditions. They need to be accessible in not just developed nations, but underdeveloped countries as well. Alginate, chitosan, collagen, and polycaprolactone have much potential in spray form. In future biological evaluation, certain parameters will be tested such as easy removability and non-traumatizing characteristics.

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