Chapter 15
Wound Healing With Herbal Excipients:
Navigating Regulatory and Ethical Landscapes

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ABSTRACT

The combination of herbal excipients and polymers, as alternatives to conventional medicines, offers the potential for a novel and effective wound healing therapeutic approach with biocompatibility, sustainability, and improved outcomes for patients. The use of herbal components derived from medicinal plants, which have anti-inflammatory, antimicrobial, and regenerative properties, combined with polymers, both natural and synthetic, as they can also affect the encapsulation of various types of therapies and create a controlled drug release system while mimicking the extra cellular matrix /wound site, heralds a new era of Herbo-polymeric technologies in wound care. Although the advancements in wound care technologies are substantial, the adoption of Herbo-polymeric technologies is hindered by a fragmented regulatory space, inconsistency in standards, and complicated ethical issues. The chapter outlines an integrated approach to explore the interdisciplinary science, formulation, as well as an analysis of the regulatory and ethical category associated with herbal and polymeric systems.

INTRODUCTION

Wound healing is a complicated physiological process (hemostasis, inflammation, proliferation and remodeling) that requires real advancement in the development of effective therapies. (Boateng & Catanzano, 2015) There has been a trend towards the use of herbal excipients, and polymers in modern medicine. These materials have biocompatibility, biodegradability and provide therapeutics for patients. (Dhivya et al., 2015) Herbal excipients (plant derived) have been found to promote wound healing, by enhancing wound repair through modulating inflammation and tissue regeneration. Polymers (natural and synthetic) are used as scaffolds and delivery systems for advanced wound care systems. (Chattopadhyay & Banerjee, 2022) While these products have great potential for wound healing, quality standards and regulatory pathways differ considerably and limit the application to clinical practices. Furthermore, there are ethical considerations with respect to using information from traditional knowledge and natural resources, including informed consent, intellectual property rights and sustainability. (Patwardhan et al., 2005) Because these products are often located in the overlap of pharmaceuticals and traditional medicine, we see the need for clear regulatory and ethical frameworks. We do intend for this review to delve into these important aspects, evaluate what currently is being done, and what that might look like to move forward.

Background on Wound Healing and Modern Therapeutics

Wound healing is an elaborate and dynamic biological process that is comprised of four overlapping phases; hemostasis, inflammation, proliferation, and tissue remodeling. (Guo & DiPietro 2010) Each of the wound healing phases must be timed precisely and coordinated with each cellular and molecular component in order to restore the skin to its previous state of integrity and function. Most acute wounds heal in a predictable time frame, whereas chronic wounds (e.g. diabetic ulcers, pressure sores, venous ulcers) often remain in a pathological- inflammatory phase of healing and thus delayed or incomplete healing. (Brem & Tomic- Canic 2007) Common treatment modalities for wounds include debridement, infection control, and moist wound dressings.

Collectively, these methods have developed to follow traditional care paths (e.g. debridement, etc.) and now use advanced therapeutic technologies (e.g. stem cells, growth factor therapies) and have improved and evolved through introducing bio-engineered skin substitutes. (Velnar et al 2009) In addition, the development of advanced wound dressings (e.g. bio-absorbable polymers, nanoparticles, antimicrobials and bioactive products) has increased treatment opportunities. Nevertheless, the cost or limited accessibility of these treatments has drawn interest in other forms of treatment that are affordable and include herbs and polymeric products/systems, even when they resemble established methods.

Phases of Wound Healing

Healing a wound is an intricate multi-stage biological process aimed at restoring damaged dermis and underlying tissue to its original state. The wound healing process includes four separate biological stages: hemostasis, inflammation, proliferation and tissue remodeling. Hemostasis happens immediately following the injury, and is the prevention of blood loss via blood vessel constriction, and clotting (Jayakumar et al., 2011). After the hemostasis phase, inflammatory phase follows and consists of the activation and recruitment of immune cells such as neutrophils and macrophages, to eliminate pathogens and debris. Inflammatory phase is followed by the proliferative healing phase in which tissue regeneration is renewed via the following processes: activation of fibroblasts, deposition of extracellular matrix, (ECM), angiogenesis, and re-epithelialization (Falanga, 2005). The final phase of tissue remodeling reinforces the repaired tissue by reorganization of the new collagen fibers, which increases tensile strength to the newly repaired skin. An organized coordination of the above four processes is critical for a well-timed and efficient healing process. Disruption of the above processes can result in chronic or non-healing wounds.

Acute vs. Chronic Wounds

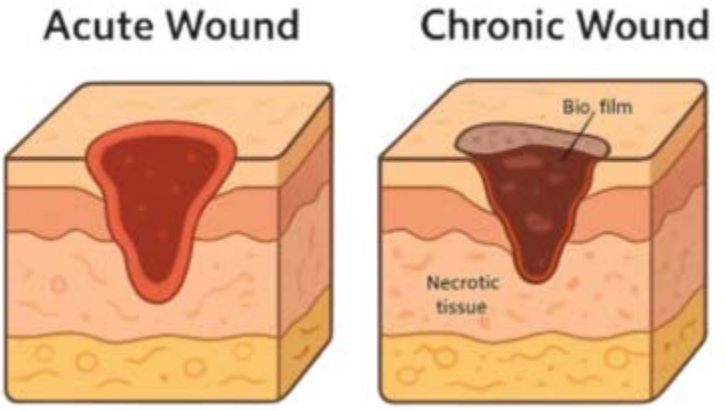
Acute wounds typically adhere to a predictable and timely healing process by cycling through the phases of hemostasis, inflammation, proliferation, and remodeling without significant interruption (Frykberg & Banks, 2015). These wounds can be related to surgical cuts or small injuries, usually heal within weeks, and follow the general plan with few negative issues when managed appropriately. Chronic wounds such as diabetic foot ulcers, pressure ulcers, and venous leg ulcers, have not been able to progress through the normal stages of healing, and are likely in a prolonged inflammatory phase (Mustoe et al., 2006). This prolonged inflammatory phase is caused by underlying conditions such as infection, ischemia, neuropathy, and systemic conditions such as diabetes, resulting in tissue break down and lack of re-epithelization. Chronic wounds are also entailed in a considerable burden on the healthcare system and on the patients due to their length of time heal, high rate of recurrence, and increased likelihood of complications. (Boateng et al, 2008). A comparative summary of these characteristics is displayed in **Table 1,** while **Figure 1** compares the healing processes of both acute and chronic wounds both to help with clinical-to-clinical reasoning.

Table 1. Comparison of acute and chronic wound healing phases

Feature	Acute Wounds	Chronic Wounds
Onset and Duration	Develops suddenly; heals within predetermined timeframe	Extended healing; lasts longer than 4-6 weeks.
Inflammatory Response	Transient inflammatory response; controlled inflammation	Continuous inflammatory response; uncontrolled inflammation
Infection Risk	Low risk with appropriate management	High risk; colonization and/or infected
Healing Outcome	Complete tissue repair and regeneration	Partial/incomplete healing
Underlying Causes	Trauma, surgery	Diabetes, ischemia and/or reperfusion; pressure; ischemia; vascular insufficiency
Histological Features	Structured phases of tissue regeneration	Nonviable material, biofilm; excessive protease activity
Clinical Management	Standard dressings and/or antiseptic	Advanced therapy methods such as debridement and/or antimicrobials.

(Winter, 1962)

Figure 1. Structural differences in healing dynamics of acute vs chronic wounds



Traditional Therapeutic Approaches

Conventional wound care methods form the cornerstone of clinical wound management and include essential practices such as debridement, infection control, and the application of moist wound dressings. Debridement the removal of necrotic or infected tissue promotes the formation of healthy granulation tissue and reduces microbial load at the wound site. The individuals who conduct infection control measures with topical antiseptics and systemic antibiotics on chronic wounds are attempting to prevent or handle microbial colonization, which could slow healing. The process of healing consists of various phases and phases of healing that are sometime exclusive to acute wounds. Dressings that retain moisture (hydrocolloid, hydrogel, and alginate) will protect the wound while allowing full cover to eliminate contamination. Moist dressings provide a good moisture balance, and research established that epithelialization occurs more rapidly in moist environments, and scarring is minimized. (Sen, 2009) This coupled with the folk antibiotic and antifungal remedies for wounds that acute acid and other wound care interventions have not only advanced positive outcomes for acute wounds, they have blazed the pathways for modern wound care approaches including bioactive dressings, and tissue engineered products characterized by pharmacological and biological principles or protein dynamics in order to facilitate the improved or enhanced healing. (Shukla et al., 1999)

Role of Herbal Excipients and Polymers in Tissue Regeneration

Herbal excipients and polymers have been shown to be excellent facilitators of tissue regeneration to the superior biocompatibility, bioactivity, and multifunctionality of these herbal excipients in wound healing. Herbal excipients of plant-derived materials such as aloe vera, curcumin, neem, and Centella asiatica, select the anti-inflammatory, antimicrobial, antioxidant, and proliferative properties of these herbal excipients that can facilitate cellular regeneration and components of angiogenesis. (Hamedi et al., 2015) These bioactive compounds will facilitate faster wound closure and also minimize scar formation and infection risks, suitable for regenerative purposes.

Polymers, both natural (chitosan, alginate, collagen) and synthetic (polycaprolactone, polylactic acid) are scaffolds and controlled delivery devices that enable a sustained release of therapeutic agents in adhesion, and tissue remodeling. (Ekor, 2014) Polymers complement herbal excipients by improving stability and solubility and improving bioavailability to phytoconstituents. The combination of herbal excipients with polymers gives rise to next gen wound care platforms like hydrogel dressings, nanofibers, and films that mimic the extracellular matrix which provides functional tissue recovery. Overall, utilizing herbal excipients and polymers in wound healing formulations offers an attractive avenue towards natural, effective, and patient-friendly regenerative therapies.

The Need for Regulatory and Ethical Oversight

The incorporation of herbal excipients and polymers to contemporary wound care can introduce significant regulatory and ethical implications to safeguard the public from harm, inefficacy, and lack of trust as with herbal product use. Herbal-based therapies used in wound care do not face the same obligations as pharmaceuticals. Herbal products often face challenges involving consistency, quality, standardization with extraction and problems with the bioactive content's consistency, due to numerous differences in cultivation, harvesting, processing (Tilburt & Kaptchuk, 2008). Statistically variability of herbal products raise issues of product accuracy, probable adverse effects, or therapeutic disposition. As a result of these shortcomings, regulatory frameworks must be more defined.

Ethically the use and sourcing of herbal materials bring about unresolvable questions regarding sustainability, equitable benefit-sharing and protection of indigenous knowledge systems. Moreover, clinical exploration of herbal and polymer interventions must still ensure informed consent, data rigour, and responsible modelling practices using animals or alternatives (Eming et al., 2014). Without definable intervention oversight there is room of exploitation, misinformation and

more harm to marginalized communities. Thus, establishing standardized regulatory practices and ethical guidelines are paramount with respect to preventing harm to patients, promoting innovative practices and ensuring international acceptance of innovations in wound care management.

Aim and Scope of the Review

This review will discuss regulatory and ethical contexts surrounding the use of herbal excipients and polymers utilized in wound healing. It is essential to contextualize their biomedical relevance, given the rising global interest pertaining to naturally derived and biocompatible materials - including herbal items - which interact with evolving regulations and ethics. (Houghton & Mukherjee, 2020) The review will document the types, sources, functions, challenges related to formulation, quality, and transition to clinical use of herbal excipients and polymers. Regulatory contexts will be focused primarily on the guidelines set out by regulatory agencies such as the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA), Central Drugs Standard Control Organization (CDSCO), and India's Minister of AYUSH. Relevant ethical aspects in regard to traditional knowledge, sustainability, informed consent, and fair access will also be reviewed (Javed et al., 2021). By considering all three dimensions - scientific, regulatory, and ethical - this review is intended to help researchers, clinicians, and policymakers make further progress on developing safe, effective, and ethically defensible wound care.

HERBAL EXCIPIENTS AND POLYMERS IN WOUND HEALING

The use of herbal excipients and polymers has drawn attention in wound healing because of their natural biocompatibility and bioactivity with low toxicity. Herbal excipients are extracted from plants that were traditionally used in wound care formulations as multi-functional stabilizers, gelling agents, permeation enhancers, and antimicrobial agents. Compounds that were formulated from herbal extracts such are mucilages, gums, and tannins didn't only help to improve the mechanical properties of wound dressings but possessed bioactive properties to facilitate healing by acting on inflammation, angiogenesis, and tissue regeneration. (Nayak & Pinto Pereira, 2006). The effectiveness of herbal-based wound products has also been enhanced with the use of natural and semi-synthetic polymers including chitosan, alginate and cellulose derivatives, through the use of controlled drug release, moisture retention and 3-D structural support (Venkatesan et al., 2017). The synergistic power of herbal bioactive and biocompatible polymers can allow for the development of the next generation of sustainable and effective wound healing systems.

Classification and Sources of Herbal Excipients

Herbal excipients are naturally derived components that originate from plant sources and are incorporated into pharmaceutical and nutraceutical formulations to provide stability, bioavailability, and therapeutic benefit without therapeutic effect. The excipients can be classified depending on their physicochemical properties and functions as binders, disintegrants, emulsifiers, thickeners, film formers, and stabilizers. Each excipient class (with few exceptions) is affixed to a specific part of a plant - seeds, leaves, bark, or roots that provide a source of gum, mucilage, starch, and resin. (Kulkarni et al., 2012) For example, gums, including gum acacia, come from exudates of trees; mucilages can come from seeds of plants, such as Plantago ovata or Hibiscus esculentus. Other important examples include starch from Zea mays and cellulose derivatives from Bombax ceiba. (Pandey et al., 2016)

A detailed overview of these classes, along with their botanical sources and plant parts used, is provided in **Table 2.** This classification helps in selecting appropriate excipients tailored for specific wound healing formulations, as the physicochemical characteristics of these substances significantly influence the product's mechanical properties, moisture retention, and drug-release behavior.

Table 2. Classification and sources of herbal excipients

Class	Example	Source Plant	Plant Part
Binder	Gum Acacia	*Acacia senegal*	Exudate (gum)
Disintegrant	Mucilage	*Plantago ovata*	Seed
Emulsifier	Lecithin	*Glycine max* (soybean)	Seed
Thickener	Pectin	*Citrus sinensis*	Peel
Film-forming agent	Starch	*Zea mays* (maize)	Kernel
Stabilizer	Cellulose	*Bombax ceiba*	Bark/wood

(Deshmukh et al., 2014)

Functional Classification of Herbal Excipients

Herbal excipients have functional classifications based on their intended functions when used in pharmaceutical formulations. There are many functional classes, with some common classes of excipients listed as binders (such as acacia gum), disintegrants (e.g., isabgol husk mucilage), emulsifiers (e.g., lecithin), thickeners (e.g., pectin), film formers (e.g., starch), and stabilizers (e.g., cellulose). The functionality of herbal excipients likely relates to their complex polysaccharide content,

glycoproteins, or proteins which provide structure for adhesion for swelling, when used in wound dressings and in topical formulations. (Mali et al., 2010)

Botanical Sources and Plant Parts Used

Herbal excipients can be sourced from a large number of plant species, and can also be harvested from many areas of the plant. For example, Astragalus species yield gums such as gum tragacanth, mucilages are produced from Hibiscus and Plantago, starches can be sourced from maize and potato, and cellulose can be harvested from cotton and fibrous wood plants. Each area of strain provides differing amounts of chemical and/or structural content, and these will impact the effectiveness of the excipient in a formulation. (Shaikh et al., 2011).

Advantages Over Synthetic Excipients

Herbal excipients are biodegradable, environmentally friendly, cost-effective compared to synthetic excipients, and generally well tolerated. Their natural origin means that they are more biocompatible and will show lower incidence of adverse reactions, which is important in wound healing when there is sustained skin-contact. In addition, some herb-based excipients exhibit inherent antimicrobial, anti-inflammatory, and antioxidant action that help produce a healing environment (Jani et al., 2012).

Considerations in Selection and Processing

The selection of herbal excipients needs to consider prophylactic qualities of the herbal excipient and combinations of formulations, as well as their own physicochemical properties, compatibility to active ingredients, and stability in formulating conditions. Processing methods and techniques (drying, making powder, purification) are important to keep their functionality and limit microorganisms. Standardization is a challenge as variables arise from the plant source, harvest season, and geographical source, putting quality control at forefront of regulatory context. (Ravikumar et al., 2013)

Natural and Synthetic Polymers: Biocompatibility and Use

Polymers, including both biological (natural) and synthetic types, play important roles in wound healing because they provide hydrogels, films, and scaffolds that assist with tissue regeneration. Biological polymers include chitosan, alginate, gelatin, hyaluronic acid, and cellulose. These polymers, derived from biological

origins, have excellent biocompatibility, biodegradability, and low antigenicity. (Ahmed, 2015), Additionally, the structural similarities of biological polymers with the extracellular matrix (ECM) allows cells to adhere, proliferate, and migrate which all are necessary processes in wound repair. There are many examples of biological polymers that assist in wound repair, and part of those processes is their nature. For instance, chitosan from crustacean shells has antimicrobial uses and supports hemostasis. Alginate from brown seaweed forms gels that are ionically cross-linked, which also provide a moist wound environment and take exudate.

Synthetic polymers are also important for their role in tissue repair and include poly (lactic acid) (PLA), poly (glycolic acid) (PGA), and polyvinyl alcohol (PVA). Synthetic polymers are different than biological polymers and offer some advantages such as mechanical robustness, structural integrity, and have defined degradation rates (Ullah et al., 2015). These types of polymers can also be fabricated at the level of the molecule which allows for degrees of freedom to meet specific physicochemical and pharmacokinetic requirements. Tempted not to, but not forgot to mention, synthetic polymers do not have biological activity and proper respects of not calling them biological. Regardless synthetic polymers are frequently utilized with bioactive compounds or natural polymers and other things to achieve a therapeutic result and reduce cytotoxicity.

The decision between natural and synthetic polymers is dependent on the application, desired healing dynamics, and prescription factors specific to the patient. A combination of both polymer types working synergistically is increasingly found in next-generation wound dressings and drug delivery systems.

Mechanisms of Action in Wound Healing

Wound healing is dynamic and multimodal. Wound healing occurs in four overlapping transition phases of: hemostasis, inflammation, proliferation, and remodeling. Each phase is characterized by unique cellular and molecular events which can be supported or augmented, by both the natural and synthetic polymers used in a variety of wound care technologies. (Balaji et al., 2016)

Hemostasis

Having an injury, blood vessels tighten up and platelets quickly join forces to form a clot that will last just a short time. As a result, the clot seals the wound and creates a place where cells can travel. As illustrated in **Figure 2,** during this stage both red blood cells and platelets are present, as are some bacteria. This process is enhanced by natural polymers such as chitosan which facilitate platelet attachment, change their activity, improve the rate of forming blood clots and add defense against

bacteria. Because of polymer use, barricades form inside the wound, protecting it from outside germs. (Chen & Abatangelo, 1999).

Inflammation

The inflammatory phase of healing is characterized by the influx of white blood cells, together with macrophages to help debride and remove debris and pathogenic agents, as well as releasing cytokines for repair. Natural polymers such as hyaluronic acid modulate inflammation through regulating leukocyte migration and cytokine expression. Additionally, polymer-based systems could be employed as a delivery mechanism for anti-inflammatory agents, whether owned vehicles that could possibly target the inflammatory site in an effort to reduce the duration of inflammation (Gurtner et al., 2008).

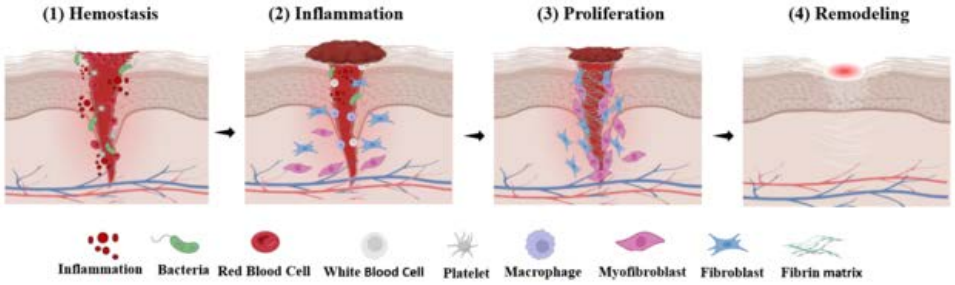
Proliferation

In this phase, the wound bed is restocked with fibroblasts, myofibroblasts, and endothelial cells, facilitating angiogenesis, ECM deposition, or re-epithelialization. Figure 1 shows cellular activity at this phase is continuous and abetted by the provisional matrix. Hydrogels from polymers such as alginate and gelatin retain a moist wound environment that is necessary for cell migration and proliferation. Synthetic scaffolds mimic the ECM and allow for the cells to anchor and grow in addition to has the ability to allow for controlled release of growth factors to increase granulation tissue (Zhao et al., 2017).

Remodeling

In conclusion, collagen is reorganized, the new tissue matures, and scar tissue forms at this final stage of repair to restore the original function of the tissue. As shown in Figure 1, the outcome of wound healing and repair is an intact wound through vascular and epidermal remodeling. Analogs like PLA and PGA will be made to reabsorb to match tissue regeneration; they provide support only as long as needed A (Middleton & Tipton, 2000).

Figure 2. Sequential cellular and molecular events in the four phases of wound healing



Recent Advances and Formulations

New technologies in wound healing have focused on the development of multifunctional and responsive formulations that incorporate the healing properties of natural and synthetic polymers with herbal bio actives, nanotechnology, and complex drug delivery systems to improve healing times, limit infection, and decrease scar tissue in a biocompatible and cost-efficient manner.

Polymeric Nanocomposites and Nanofibers

Electrospun nanofiber scaffolds have become the most promising wound dressings because they are built of polymers that mimic the structure of the body's native extracellular matrix, and they are designed to allow for a controlled delivery of herbal therapeutics. Commonly, natural polymers such as gelatin, chitosan, and cellulose derivatives are then blended with synthetic polymers like polycaprolactone (PCL) or polylactic acid (PLA) to develop hybrid nanofibers. For example, effective herbal agents may include curcumin or neem extract, as well as centella asiatica or aloe vera, and functional creativities include antimicrobial, anti-inflammatory, and antioxidant activities. (Mogoşanu & Grumezescu, 2014)

Stimuli-Responsive Hydrogels

Recent advances in responsive smart hydrogels that can be activated electrochemically, pH, temperature, or enzymatically, could allow the hydrogel to respond to bioactive compound delivery in a wound-specific manner. A pH-responsive hydrogel that has either quercetin or curcuminoids from turmeric altered the rate release of bioactive compounds between infected and non-infected environments (to increase the therapeutic specificity of the plant extracts) such as quercetin. These active

hydrogels typically utilize modified hyaluronic acid, poly(N-isopropylacrylamide) or carboxymethyl cellulose as the polymer base materials (Liu et al., 2017).

Herbal-Polymer Hybrid Films and Membranes

Film-forming polymers containing herbal extracts are used in the way of semi-occlusive dressings that can create moisture and provide NATURAL antimicrobial activity through herbal loading. Chitosan-based films load Calendula officinalis, Azadirachta indica (neem), or tea tree oil and have significant activity against common wound pathogens, such as S. aureus and P. aeruginosa, and also provide epithelialization and angiogenesis support (Iordache et al., 2022).

Injectable and Sprayable Formulations

Injectables hydrogels and spray on polymers are becoming more common for irregular/deep wounds. The majority of these systems can quickly form an in-situ matrix to cover the wound, promote tissue growth and deliver a drug dose intermittently. Alginate based injectable gels containing plant polyphenols or bioflavonoids are in active development given their anti-inflammatory and pro-healing function.

3D-Bioprinted Skin Substitutes

Moreover, new 3D-bioprinting allow for researchers to create skin constructs from bioinks based on natural polymers (gelatin, collagen and fibrin) and herbal induced growth enhancers. Engineered skin grafts show great potential especially towards full-thickness wounds and burns, with broader surface area and better integration and vascularization.

Challenges in Formulation and Standardization

Polymeric wound healing systems provide an important opportunity for therapy, in particular, when combined with herbal excipients, but much work is still needed to optimize formulation and reproducibility, safety and regulatory issues prior to being able to take these from a laboratory to a clinically approved product.

Phytochemical Variability and Standardization Issues

One major challenge faced when formulating polymeric herbal wound dressings is the wide variability in the composition of herbal excipients. The phytochemistry of herbal excipients can be affected by several ecological factors, such as plant

species, soil, climate, and cropping time. Even the extraction method and solvent system can influence the concentration of the bioactive constituents of the herbal excipients. The wide variability in phytochemistry presents an obstacle to batch-to-batch consistency and reproducibility of therapeutic effects. (Kunle, Egharevba, & Ahmadu, 2012). Unquestionably, it is difficult to standardize herbal products in polymer matrices, but the multicomponent nature of herbs complicates standardization even more. These inconsistencies create significant hurdles for quality control and regulatory approval.

Formulation Compatibility and Technical Limitations

When paired with polymeric carriers, there are many obstacles to formulate a product containing herbal extracts because of chemical incompatibilities. Many of the phytochemicals derive from herbal materials, are sensitive to heat, light, and/or pH, and consequently can lose their therapeutic action during processing. The challenges in achieving optimal stability and sustained release when using hydrogels, films, or nanofibers is often complicated. The poor solubility and bioavailability of herbal actives diminishes therapeutic action. While still retaining the integrity of structures and functional properties is essential; scaling up production remains a significant barrier. These limitations create obstacles for formulation development as well as the translation to industry. (Boddupalli & Kataria, 2021)

Regulatory, Manufacturing, and Clinical Barriers

The regulatory ambiguity of herbo-polymeric wound care products as drugs, devices or combination products creates difficulty in the market place, and this ambiguity occurs at multiple levels. The lack of harmonization of herbal and polymer regulations adds another layer of complexity. Manufacturers also face challenges in regulatory consistency, compliance with GMP regulations, strong quality control standards, and limited clinical validation, there are few formal, well-designed clinical studies documenting product effectiveness. All of these issues affect both the broader acceptance by health organizations and its economic attractiveness to marketplace access. For the successful commercialization of herbo-polymeric products, it is imperative that these challenges are identified and addressed (Patel & Patel, 2021).

REGULATORY PERSPECTIVES

Herbo-polymeric wound care products are subjected to regulatory ambiguity, existing somewhere in the distinction of drugs, devices, or cosmetics, by their dual

nature when offering care. The lack of harmonized global guidelines complicates approval, especially with herbal regulations and polymer technology not being aligned. Validation against GMP processes, quality control, and clinical validation are essential yet remain a barrier achieving the level of expectation related to commercializing such products. Regulatory pathways that are harmonized with respect to specific products are an opportunity to overcome barriers to global commercialization. (Langwick, 2011)

The different national frameworks for the regulatory approval of Herbo-polymeric wound care products reflects differences in the complexities of classification and the absence of harmonized international guidelines.

In the US, the Food and Drug Administration (FDA) divides products by the primary mode of action. Herbo-polymeric formulations can be regulated as a drug, device or combination product under 21 CFR part 3. Investigational New Drug (IND) and New Drug Application (NDA) filings will be required for herbal actives that have therapeutic claims, while the polymers used solely as 'carriers' will need to show safety and biocompatibility. The FDA's Guidance for Industry: Botanical Drug Development discusses the clinical and quality data necessary to support the herbal components. (FDA, 2020)

In the European Union (EU) herbal medicines and herbal medicinal products are governed by the Committee on Herbal Medicinal Products (HMPC) at the European Medicines Agency (EMA) via the Traditional Herbal Medicinal Products Directive (2004/24/EC). This framework creates pathways for registering traditionally used herbal products; however, there is presently no guidance on polymeric based systems. In the event polymeric systems come to fruition, the possibilities under Advanced Therapy Medicinal Products (ATMP) or Medical Device Regulation (MDR) regulations would likely apply based on the mechanism of action and intended use. (EMA, 2004)

A two-structured regulatory framework for India is existing. CDSCO (Central Drugs Standard Control Organization) regulates modern drugs and delivery systems under the Drugs and Cosmetics Act, 1940, while AYUSH regulates traditional systems of Ayurveda, Unani and Siddha. Herbo-polymeric products are caught in a regulatory grey area where the active herbal ingredient is covered by AYUSH and the polymer component is regulated by CDSCO, necessitating cooperation between the two regulators (Ministry of AYUSH, 2021).

In a broad sense, the absence of coherent regulatory principles between CDSCO and Ministry of AYUSH imposes considerable barriers to global commercialization. Developers of Herbo-polymeric products are faced with two sets of overlapping compliance obligations and administration that takes longer- and allows for different definitions of quality standards for herbal extracts, safety for polymers, and methods of compliance in product labelling (Parasuraman, 2012).

Regulatory Classification: Drug, Device, or Combination Product

Given their hybrid nature, it can be difficult to classify Herbo-polymeric wound healing products under regulations. These systems can consist of a bioactive herbal extract combined with a polymeric carrier or vehicles (hydrogels, nanofibers or films) – both of which can be used therapeutically or as a physical structure.

The classification in the United States will come from the FDA based on the primary mode of action (PMOA). If a product produces a therapeutic effect from the herb, it would be classified as a drug. If the effect is physical (for example barrier or scaffold), the product would be classified as a medical device. If both components independently contribute to the therapeutic effects of the product, the product includes drug and device components, making the product a combination product (21 CFR Part 3). The classification ultimately determines the route of regulation, as it is critical in pre-market submissions (for example, IND, NDA, or Premarket Approval (PMA)) depending on the classification.

A similar framework is present in the EU. The classification under the Medicinal Product Directive (2001/83/EC) or Medical Device Regulations (EU 2017/745) depends on the intended purposes and mode of action of the product. Combination product is assessed on ad-hoc basis, and uncertainty remains where herbal ingredients are added within polymeric carriers, without a well-defined pharmacological mode of action amongst the ingredients.

In India, there is no regulatory authority definition on combination products. Herbal actives may be dealt with under an AYUSH jurisdiction, while the polymeric carrier may be reviewed via CDSCO. The presence of two authorities creates and generates delay often resulting in inconsistencies in terms of regulatory arrangements, notably on new formulations in wound care that are outside the normal description usage indication bounds.

This ambiguity in classification has implications beyond regulatory route - i.e. requirements for clinical evaluation, labelling, safety testing and GMP will all be influenced. The absence of clear global standards for these hybrid systems prevents innovation and delays product development.

Quality Control and Standardization Requirements

Quality assurance and standardization of Herbo-polymeric wound care systems, or hybrid products, represent a formidable regulatory and formulation challenge. On the herbal side, extractable compounds vary due to the phytochemical nature of plants and their respective genotypes, environmental factors, harvesting and processing conditions. As such, validated chromatographic and spectroscopic methods

(e.g., HPLC, NMR, LC-MS) must be used consistently to standardize bioactive constituents and reproduce an identifiable product. (Mukherjee et al., 2011)

On the polymeric front, carriers frequently must meet demanding mechanical, physicochemical and release profile specifications. For example, parameters such as porosity, swelling index, degradation rate and encapsulation efficiency must factor into evaluating performance and safety. (Patil et al., 2009) Ideally, where herbal and polymeric components interact, both components should be considered in compatibility and accelerated stability studies to ensure stability and therapeutic efficacy, to ICH specification.

Regardless of advances in analytical techniques - the absence of harmonized global standards for hybrid products remains a debilitating bottleneck. Quality benchmarks will differ according to regulatory agency requirements; furthermore, regulatory agency specifications most often focus on either herbal or polymeric components and not both in unison. This gap increases the burden on manufacturers to develop in-house validation protocols and ensure robust, GMP compliant fulfilment of processes.

Clinical Trial Regulations for Herbal and Polymer-Based Therapies

Regulatory considerations impede the clinical assessment of Herbo-polymeric wound care products in an inconsistent and rapidly changing regulatory climate. Herbal medicines were all assessed by ethnomedical use in the past, and now are being asked to provide evidence through RCTs and pharmacovigilance data. Designing an RCT for an herbal product is difficult since the composition can vary from product to product, there are not regulated or standard doses, and blinding or introducing a placebo is challenging (Goyal & Singh, 2019).

When combined with polymeric delivery systems like hydrogels, films or scaffolds used to deliver the herbal components, the regulatory issues become more complicated due to the combination device status. The majority of carriers are made from synthetic or biocompatible polymers, but all systems must adhere to Good Laboratory Practice (GLP) and Good Clinical practice (GCP) guidelines regardless. Toxicological and safety data must be provided before clinical applications. All systems require either device or drug specific approval protocols determined by a regulatory body like the FDA or EMA.

The challenge is compounded in countries like India where regulatory frameworks for AYUSH and herbal products require registrants to provide a clinical trial registry with the Clinical Trials Registry India (CTRI) and require PMT for Ayurvedic or herbal product registrations. There is currently no comprehensive regulatory framework for combination systems such as a Herbo-polymeric product

incorporating herbal bio actives incorporated in a polymer matrix (Patwardhan et al., 2015). There is little clarity for registrants about the pathways on timelines or documentation to assess combination systems involving herbal bioactive embedded in polymer matrices.

Post-Market Surveillance and Compliance Challenges

The role of post-market surveillance (PMS) is fundamental to assuring the long-term safety and efficacy of Herbo-polymeric wound care products. These systems can fall into regulatory categories that overlap herbal, medical device or combination product, associated PMS protocols can be inconsistent and fragmented. Unlike mainstream pharmaceuticals, herbal products are inherently less stable due to batch variability and brand contamination that may not come to light until they are available for consumers. As such, strong pharmacovigilance should include ongoing monitoring of reported adverse events and product quality as products fall into various states of distribution (Barnes 2003).

Many countries do not have organized systems in place for ongoing monitoring of herbal or combination therapies after approval. Although some systems do exist, such as the AYUSH pharmacovigilance centers in India, and FDA MedWatch program in the USA, under-reporting of adverse events continues because of factors such as under-recognition of side effects, the poor understanding of therapeutic range, and lack of awareness among users and practitioners. After approval, establishing a commitment to maintain compliance with Good Manufacturing Practices (GMP) may also present challenges for manufacturers, particularly for those using seasonal plant materials or employing more artisanal production.

Further complexity is added by inconsistencies or instability in the supply chain that can introduce badly sourced build material or changes to formulations that culminate in products being non-conforming to the safety and regulatory requirements of the original manufacturer and the product approval. Without the benefit of continuous Quality audits, real-world data collection, and increased education stakeholders, it will be difficult to fill this gap with consumer understanding and confidence.

ETHICAL CONSIDERATIONS

There are some ethical issues associated with Herbo-polymeric wound management, which include ensuring an informed consent process, particularly in clinical trials in traditional remedies and traditional practices where participants may not fully appreciate the inherent risks. There is also the potential to undermine public confidence from misleading claims of efficacy when there is no sound clinical ev-

idence to support those claims. Participants are entitled to fair benefit-sharing with indigenous communities, per the Nagoya Protocol, but that may not be strongly considered by researchers. Sustainability in harvesting any herbal sources is implicated by ethical obligations with respect to the environment. Ensuring there is transparency in labelling and marketing is part of the ethical obligation to protect consumers. Ethically, the oversight of this work must be investigated by multidisciplinary review boards and committees. The regulatory framework will need to adapt or draft regulations to these emerging bioethical areas. (Cohen et al., 2011)

Importance of Informed Consent

Informed consent is vitally important for respecting participants' autonomy in clinical research. In Herbal-based research, there often may be a tendency that products are safe because of their use over time and may lead participants to make assumptions. Many of these herbal products have not been subjected to questioning and clinical trials and invariably ethical oversights can occur when researchers have not taken the time to describe in detail the investigational status of the intervention. (Bhatt, 2010)

Unique Challenges with Herbal and Polymeric Formulations

Herbal extracts vary in composition depending on the source plant, season, and extraction method, increasing the unpredictability of drug delivery and efficacy when considering starting with polymer systems such as nanogels or films. Participants should also be made aware of the potential for new drug–carrier interactions and the limited available history of the same. (Sahoo, Parveen, & Panda, 2008) It is critical to highlight the increased potential for complications in consent from these interactions, an additional layer of complexity in ensuring clear communication during the consent process.

Support for Comprehension with Diverse Populations

Having a legal form of informed consent is one thing, but a thorough, comprehensive consent process must also incorporate culturally appropriate strategies. For participants from areas where herbal medicine is a cultural norm, they may never have been exposed to a clinical study protocol or may demonstrate skepticism of a biomedical framework. Use of vernacular languages, images, and the support of community leaders will aid in participants ensuring their understanding and voluntary participation. (Srinivas, Anand, & Nath, 2019)

Continuous Consent and Ethical Oversight

Consent is a feature of ethical responsibility that must be maintained. During the conduct of trials, researchers may find new adverse effects or product interactions which mean they must obtain new consent from the participants. Ethics review boards must maintain ongoing scrutiny of consent procedures, especially in cases involving new technologies and old remedies. (Langat, 2005) Such conversations foster trust from participants and are crucial to the credibility of the study.

Ethical Use of Traditional and Indigenous Knowledge

Application of traditional and indigenous knowledge (TIK) when designing Herbo-polymeric technologies for wound care offers astonishing possibilities while simultaneously creating complicated ethical issues. Communities have for many years preserved intricate and valuable medicinal knowledge, but their sponsors or contributions remain largely unrecognized or utilized for unfair exploitative practices during studies and commercial use. Creating respectful relations, obtaining prior informed consent, and designing fair benefit-sharing agreements are vital to protecting the dignity and rights of the holders of knowledge. In the case of TIK, some international documents like the Convention on Biological Diversity and Nagoya Protocol make it easy to apply them ethically in modern biomedical practices. (Bannister, 2014)

Respecting Cultural Heritage and Intellectual Property

The integration of indigenous and traditional knowledge into modern Herbo-polymeric wound care must be carried out with the most respect for the cultural tradition from which such knowledge originates. This implies recognition of traditional healers and communities as legitimate holders of knowledge and a refusal to appropriate their knowledge without their consent or acknowledgment. Ethical guidelines should provide that knowledge is not desorbed from its context or utilized in a manner that breaches cultural protocols. (Posey & Dutfield, 1996)

Benefit-Sharing and Community Consent

Ethical bioprospecting is mandated by prior informed consent (PIC) from traditional communities and equitable access and benefit-sharing (ABS) regimes. These are provided in the Nagoya Protocol, where benefits derived from the commercial or scientific use of traditional knowledge must be shared equitably. These benefits

include monetary benefits, capacity development, and participation in the research process. (Morgera et al., 2012)

Avoiding Exploitation in Commercialization

Commercialization of herbal products derived from indigenous knowledge without community involvement or recognition is considered unethical exploitation. Many companies in the past have profited from such knowledge without bringing back any value for the source communities. To avoid the exploitation of communities and ensure that innovation is sustainable, transparent agreements must be in place, with legal protection of community intellectual property and ethical review mechanisms. (Shiva, 2001)

Sustainability and Environmental Ethics in Sourcing

Sustainable sourcing practices for raw materials great biodiversity and long-term existence of medicinal plants upon which Herbo-polymeric wound care products depend are imperative. Exorbitant harvesting, habitat obliteration, and non-sustainable agricultural methods are threats to the survival of agents that are valuable, including ecological upliftment and training for livelihood to human communities. Ethical sourcing entails adherence to environmental ethics with conservation and responsible harvesting and further support for regenerative cultivation methods. Supply chain transparency along with respect for international environmental agreements are also critical to lessening negative impacts and augmenting social equity among indigenous and local communities dependent on these natural resources. (Smith & Berkes, 2018)

Conservation of Medicinal Plant Biodiversity

The extensive demand for natural wound care ingredients has caused severe strains on medicinal plants through excessive harvesting which endangers biodiversity and places endangered species at risk. The protection of plants requires methods that support sustainable harvesting along with endangered species cultivation and natural habitat conservation. These methods support the creation of durable plant populations for upcoming times without disrupting ecosystem equilibrium. (Ticktin, 2004)

Responsible Harvesting and Supply Chain Transparency

The ethical standard for sourcing herbal materials depends on the disclosure of both collection methods and the specific origin of plant materials. The practice

of responsible harvesting involves limiting the overall collection volume and stopping harmful extraction practices and following natural growing seasons. Product accountability and the ability to develop consumer trust in genuine sustainable products need systems that provide tracking and certification. (Marshall et al., 2006)

Supporting Indigenous and Local Communities

Environmental ethics expand their study area from ecological systems to address the social fairness needs of communities who depend on growing medicinal plants. Through benefit-sharing programs and fair-trade operations and capacity-building activities indigenous and rural communities develop improved resource management practices which support their economic growth and environmental sustainability. The implementation of collaborative stewardship models leads to industry stakeholders and traditional knowledge holders developing relationships based on mutual respect. (Berkes, 2009)

Compliance with International Environmental Frameworks

The fulfillment of international treaties including the Convention on Biological Diversity (CBD) and the Nagoya Protocol stands as a critical requirement for establishing sustainable and fair plant genetic resource utilization. The frameworks establish regulations to protect resources while supporting sustainable usage and fair benefit distribution thus developing a legal and ethical foundation for herbal-polymeric wound care product development. (Convention on Biological Diversity Secretariat, 2011)

Animal Ethics and Alternatives in Preclinical Testing

The advancement of Herbo-polymeric wound care products demands preclinical evaluations which confirm their effectiveness along with safety for human trials. In the past the research community relied on animal models to investigate biological reactions during this developmental stage. The scientific testing limitations combined with ethical animal welfare concerns have motivated researchers to discover alternative evaluation methods. Scientists dedicate their research efforts to establish non-animal models that improve ethical requirements while making their predictions better through the 3Rs guidelines of Replacement, Reduction, and Refinement. The field of preclinical research faces a major obstacle when researchers need to comply with regulations while maintaining ethical standards.

Ethical Concerns in Animal Testing

The standard preclinical test method uses animal models to evaluate Herbo-polymeric wound care products throughout their safety, efficacy, and biocompatibility assessments. Research testing follows ethical principles that mandate researchers use the least number of animals possible while controlling animal discomfort to reach scientifically valid results. The Institutional Animal Care and Use Committees (IACUCs) create regulations to maintain humane treatment practices while reducing the number of animals used for experimentation. (Steneck, 2006)

The 3Rs Principle: Replacement, Reduction, Refinement

The 3Rs Principle establishes standards that guide ethical animal research practices. Ethical animal research moves forward under the 3Rs framework by:

- **Replacement:** Researchers should prioritize non-animal testing methods which include in vitro assays along with computer simulations and organ-on-chip systems.
- **Reduction:** Conducting studies which require the smallest number of animals.
- **Refinement:** Researchers improve their protocols to decrease both pain and distress levels. (Morton & Griffiths, 1985)

Emerging Alternatives in Preclinical Testing

Biotechnology progress has created three promising substitute methods to test products that do not involve animal research. The implementation of these methods handles ethical problems and generates more human-relevant data which leads to enhanced predictability for herbal-polymeric formulations. (Russell & Burch, 1959)

Regulatory Acceptance and Challenges

The acceptance of substitute methods continues to face regulatory agency requirements for using animal data in approval processes. The process of linking these two elements requires both new proof for alternative models and adjustments to regulatory standards to include scientific and moral advancements. The adoption of animal-free testing strategies requires researchers and industry leaders to work alongside regulatory agencies through collaborative efforts. (Hartung, 2008)

Data Integrity, Transparency, and Equitable Access

The development of Herbo-polymeric wound care products depends on maintaining data integrity across the research and development lifecycle to establish trust and drive product innovation. Reliable and openly accessible data enable scientific rigor while supporting regulatory compliance and informed clinical decision-making. These innovations must provide equitable access to all individuals to prevent exclusive benefits from reaching underprivileged communities worldwide. The fulfillment of these ethical responsibilities leads to better public health outcomes through both accountability and social justice development for therapeutic innovations.

Importance of Data Integrity

The study shows that preserving data integrity serves as essential for developing herbo-polymeric wound care products. Scientific validity together with regulatory approval depends on the foundation of accurate and complete and reliable data. Trust erosion and market exposure of unsafe products occur when data undergoes manipulation or selective reporting or falsification. Researchers need to maintain strict data collection and storage and analysis protocols that guarantee both reproducibility and accountability. (Balls et al., 2012)

Transparency in Research and Publication

The research community demonstrates transparency through the public availability of research protocols and datasets and results which anyone can verify to develop scientific knowledge. Publication bias decreases while stakeholders like clinicians and regulators gain informed decision-making capabilities through transparent reporting. Research transparency improves through open-access platforms and clinical trial preregistration which becomes vital when herbal medicine research encounters difficulty in validating real efficacy because of conflicting data and undisclosed proprietary formulations. (Nosek et al., 2015)

Equitable Access to Innovations

Equitable access means that Herbo-polymeric wound care developments reach people from all walks of life especially those in underprivileged and underfunded areas. The system requires equal pricing structures and available products in low-income areas alongside culturally relevant product designs. Health equity throughout the world will improve through the progress of new products that combine tradi-

tional knowledge with modern innovations while avoiding the deepening of current disparities. (Peters et al., 2019)

Intellectual Property and Sharing of Benefits

The protection of intellectual property rights requires a delicate balance with the moral obligation to distribute advantages. Patents act as a catalyst for innovation, while at the same time restricting and raising costs. Ethical principles advocate for negotiated licensing and patent pools and engaged licensing through public-private partnerships, which would allow widespread availability of products, while still protecting the rights of every inventor. (Tobin & Lewison, 2011)

Role of Regulatory and Funding Bodies

The combination of regulatory agencies and funding institutions functions as the cornerstone to safeguard data reliability and transparency and equal access through the enforcement of standards and data sharing requirements and provision of support for underserved population programs. Their oversight enables commercial interests to harmonize with public health targets which leads to the translation of innovation into practical benefits. (Ioannidis et al., 2014)

CURRENT CHALLENGES AND FUTURE PROSPECTS

The use of herbal therapeutics through polymer-based delivery systems has great potential for integrating into a future advanced wound care process; however, there are numerous challenges for developing and commercializing Herbo-polymeric wound care products. These challenges include specific technical difficulties related to stabilizing the formulation, ensuring bioavailability, and regulatory obstacles, as well as ethical issues related to sustainability and traditional knowledge of herbs. However, present trends in material science, biotechnology, and regulation, together with increased awareness of and involvement in integrative medicine and local cooperation, provide the scope to push ahead in our present limitations. (Gatt et al., 2024) Therefore, there is a scope for transformational development in the sector, to encourage the advancement of more efficient, secure, ethical, accessible, and effective wound healing therapy.

Gaps in Global Harmonization of Herbal Product Regulations

Due to differences in culture, law, practice, and science, regulation of herbal products really varies all over the world. This lack of universal standardization poses problems for the Herbo-polymeric products trying to obtain regulatory approval and commercialize in different markets. Differences in classification, supervision of clinical trials, quality control practices, and surveillance of the market after a product's release create obstacles to reliable testing of the safety and efficacy of a product. **Table 3** presents major regulatory variations between leading regions, focusing on these variances in terms of classification, quality standards, clinical evidence, and pharmacovigilance. Harmonization of these regulatory elements is vital to support global trade, safeguard consumers, and foster innovation in herbal therapeutics. (Zhang & Li, 2022)

Table 3. Summary of key regulatory differences in major regions

Regulatory Aspect	USA (FDA)	EU (EMA)	India (AYUSH)	China (NMPA)
Division of Tasks	Diet Supplement or Drug	Drug Traditional Herbal Medicinal Medicine or Drug	Traditional Medicine	Traditional Chinese Medicine
Quality Assurance	Good Manufacturing Practices, Standards of USP-to-USP documents	UA Monographs Self passports	AYUSH Pharmacopoeia standards	Chinese Pharmacopoeia
Research of Clinical Practices	Multi-lateral reproducible tests with “Clinically Controlled Test” defined as RCT for drug removed	Rigorous Constraining supporting traditional use	Relies heavily on empirical evidence	Combination of traditional usage and clinical evidence
Surveillance of the Market after Its Launch Types and Techniques	Active EU Pharmacovigilance System	Regularly Check required Active Restriction	Passive surveillance	Frontline emerging recent years

Diverse Regulatory Classifications

Across the world, herbal products are gone through different stages of their regulatory classifications. In some countries, these products are treated as dietary supplements, which results in a more relaxed distribution, while in other countries, they are regarded as traditional treatments, pharmaceutical goods or even cosmetics. This regulates how much attention is paid to the product's safety, efficacy, and marketing claims. This fragmentation of classification poses complex challenges in

the product development and approval processes for manufacturers, as a formulation that is compliant with one country's regional regulations may need drastic changes to meet another's. In addition, vague capturing definitions or boundaries, such as combination products containing herbal materials and polymers, add to pre-existing regulatory uncertainty concerning claim substantiation, increasing the cost and time for market entry. (Chan & Leung, 2021)

Inconsistent Quality Control and Standardization

Quality control for herbal products is a major concern worldwide, primarily because there aren't any standardized guidelines in place. When it comes to sourcing raw materials, several factors come into play, such as the challenges of identifying different plant species, their geographic origins, and the conditions under which they're harvested. It's important to note that there can be quite a bit of variation in the phytochemical profiles and potency of these substances. The extraction methods can differ significantly, which in turn impacts the content and qualities of the active ingredients. Regarding the evaluation of purity, the analytical techniques and tests may vary considerably between different pharmacopeias or government agencies. Such inconsistency in the monographs or standards of the majority of herbal products becomes a challenge for manufacturers attempting to address varied regulatory quality standards. Such inconsistencies may risk product safety and efficacy, make consistency assurance across batches more cumbersome, and complicate the regulation submission process. (Goyal & Bhattacharya, 2022)

Varied Clinical Evidence Requirements

Different countries have different requirements for clinical evidence when registering herbal products. Some regulatory bodies require RCTs, pharmacokinetic studies, and extensive clinical trials, while others impose stringent requirements similar to those for proprietary medicines and rely on well-documented ethnobotanical evidence and traditionally used evidence as proof of safety and efficacy. Such differences pose considerable time and financial challenges for manufacturers that need multi-regional registration. The fact that clinical trial standards for Herbo-polymeric products are also lacking contributes to the difficulty in study design and comparability. This heterogeneity thus prevents immediate patient access to new herbal medicines and inhibits their further incorporation into mainstream medicine. (Martinez et al., 2020)

Post-Market Surveillance and Pharmacovigilance

Systems to keep an eye on herbal products after they hit the market aren't well-developed and differ from country to country. To watch out for safety, we need reliable ways to follow identify, and tell others about side effects or quality issues once a product is on the shelves. In many places, there's no need to monitor products after they're sold, or the ways to report problems are all over the place. This means fewer people speak up about issues, and it takes longer to find out when something's not safe. This has sometimes led to product recalls or punishments from regulators after harmful effects come to light. Also, the complex nature of herbal mixes often with many ingredients, makes it hard to pinpoint the cause in side effect investigations. To make sure products stay safe keep public trust, and help regulators make choices, we need to beef up PMS and align safety monitoring across the board. (Singh & Gupta 2023)

Ethical Oversight in Developing Nations

This is to ensure that the research and development of herbal as well polymer based wound care products are conducted in a manner that met both international ethical standards has to be accompanied by appropriate oversight from an ethical standpoint in developing nations. Limited governance of course infrastructure, resource constrains and sociocultural disadvantages are what hit the best hardest. Closing these ethical gaps is necessary to safeguard participant rights and transparency as well as equitable benefit-sharing.

Risk of Exploitation and Inadequate Informed Consent

Critical deficiencies in developing nations are the lack of Institutional Ethics Committees (IECs)/Research Ethics Committees (RECs) which prevents meaningful ethical oversight on clinical research. In some areas, these are under-staffed committees that compromise availability of skilled personnel and are not well supported in operation. In many cases this results in delayed reviews and inadequate oversight of study designs. Also, the potential for conflicts of interests and questionable decision-making without true legislative independence is noted. Those failings ramp up the likelihood that human subject research will be done improperly. The absence of well-functioning IEC systems may leave participant rights and safety unsecured. This is essential to achieve compliance with international norms, ethics infrastructure strengthening. (Nyika et al., 2009)

Lack of Regulatory Harmonization and Legal Frameworks

No country will have unified legal/ regulatory frameworks for the research with herbal medicine and traditional knowledge in low- and middle-income countries. This results into Research Participant protection inconsistent with the welfare protection of Ethnic communities. The absence of cohesive policies can be confusing and diffuse ethical oversight. This cause traditional knowledge holders to not be fairly acknowledged or rewarded. It is critical to expand and democratize regulation (Homedes & Ugalde, 2005)

Inadequate Community Engagement and Benefit-Sharing

Ethical oversight in peer-reviewed research of developing nations often confines local communities at every stage as passive subjects of studies. Traditional healers and native knowledge holders are often left out of consultations as well decisions. This lack of engagement does not engender trust and reciprocity. Ethical issues arise around exploitation as benefit-sharing is almost never on the agenda. As this undermines community support and long-term collaboration generated from such practices. Engagement pathways need to be inclusive and transparent. (Tindana et al., 2007)

Technological Advancements in Regulatory Monitoring

Technological innovations are reshaping the landscape and practice of regulatory monitoring in healthcare, pharma, herbal/ polymer wound care products. Digitalization: fresh transparency on pre and post market surveillance for compliance. This is particularly useful in low-resource settings were regulatory bodies often battle lack of infrastructure, and workforce. Point subtopics: Technical interventions for Regulatory Oversight.

Digital Platforms for Regulatory Submissions

E-submission processes help to automate the approval process by submitting required documents electronically and providing centralized data access via digital platforms. Such systems mean less paper, less human error and quicker regulatory clearance. In terms of accountability and efficiency, real-time updates also increase transparency. Investors' better coordination can be achieved by the improved communication between stakeholders. This is to modernize the ever-evolving regulatory practices globally. (WHO, 2021)

AI and Machine Learning in Pharmacovigilance

Artificial intelligence (AI) and machine learning (ML) are currently transforming pharmacovigilance with faster detection of safety signals. They enable these tools to sift through massive adverse event data with a great degree of accuracy. Used to highlight the drug-herb interactions that could be possibly missed by manual review. AI systems are used in predictive modeling for the early signal of potential occurring risks. It makes the regulatory response mechanisms more effective. As a result, these technologies enhance the safety of natural and synthetic drugs. (De Freitas et al., 2020)

Blockchain for Supply Chain Integrity

Supply chain transparency and traceability can be considerably enhanced in the field of herbal products due to the extensive use of Blockchain technology. Cryptography secures a public, immutable and scalable ledger to register every transaction done on it and store that data cannot be changed or tampered. This assist is authentic product verification throughout production and warehousing. Similar to herbal markets, blockchain is also essential for fraud intervention and anti-counterfeiting. With that, only the identified and ethically sourced ingredients are being used. Proves Compliance with regulatory and sustainability standards that manufacturers can Share Blockchain overall helps safer herbal delivery. (Kumar et al., 2021)

Mobile and Cloud-Based Monitoring Systems

Mobile and cloud-based systems make it easier to keep an eye on clinical trials and post-market activities in real-time. Healthcare workers and the public can quickly report problems, even from remote areas. This boosts safety checks and makes regulations run smoother. With cloud storage, accessing data is both simple and secure. Overall, these tools update the way we do monitoring. (Danzon & Keuffel, 2019)

Recommendations for Policymakers and Researchers

For developing Herbo-polymer wound care products ethically and effectively, it's key for policymakers and researchers to team up. We need to get regulatory rules to line up worldwide to make approvals easier. It's really important to boost research resources, especially in developing areas, so we can build strong clinical evidence. We should focus on ethically sourcing materials and sharing the benefits with local communities. Backing sustainable farming and fair trade is really important for keeping our environment safe. When we come together and combine old farming

practices with new science, we can help ensure that everyone can easily get the treatment they need.

Promote Global Regulatory Harmonization

Policymakers need to work on aligning herbal product regulations across different countries. Right now, the varying classification systems and rules make it tough to trade and innovate globally. Creating common standards for quality, safety, and testing is really important. Groups like the International Council for Harmonization can help with this. Having one set of rules would cut down on duplication and help get products to market faster, which would also increase safety and build consumer trust. (Van den Berg et al., 2020)

Strengthen Research Capacity in Developing Regions

Improving research skills in developing areas is crucial for advancing Herbo-polymeric wound care. A lot of low- and middle-income countries deal with issues like poor infrastructure, not enough skilled workers, and limited research funding. Putting money into training, lab tools, and clinical trial networks can really help improve the quality of research. Teaming up with international groups can share knowledge and inspire fresh ideas. Sticking to standard research methods makes it simpler to compare data and get regulatory approval. These steps can lead to better healthcare solutions for everyone. (Chaturvedi et al., 2019)

Encourage Ethical and Sustainable Sourcing

Promoting ethical and sustainable sourcing is essential for biodiversity conservation and respect for the indigenous knowledge systems. There should also be some fair-trade covers in higher levels of government and the industries as a means to control overexploitation of medicinal plants. The Nagoya Protocol provides a system for fair benefit-sharing and the protection of community rights. Ethical sourcing can also help in maintaining traceability and product integrity." These methods help to identify trust with local communities and guide long-term ecological stewardship. (Ten Kate & Laird, 2018)

Foster Interdisciplinary Collaboration

The development of Herbo-polymeric products for injured skin depends greatly on close cooperation across multiple fields. Input from researchers, traditional practitioners, government bodies and others in the field can improve both making and

studying health products. Using the knowledge of traditional practitioners makes traditions meaningful and encourages everyone to act ethically. Early regulations guide researchers so the products comply with approval standards. Working together encourages more people to trust and use the new technology. Shared problem-solving platforms can speed up the process of bringing discoveries into actual products. They help close the divide between scientific medicine and older medical practices. Joining forces inclusively leads to safer and more fair healthcare. (Canigueral et al., 2021)

Future Scope for Integrative Ethical-Regulatory Models

Increased complexity of Herbo-polymeric wound care systems underscores the imperative for synergistic ethical and regulatory frameworks. Emerging models need to harmonize scientific progress with sensitivity towards traditional knowledge, cultural values, and environmental stewardship. An integrated, patient-oriented system that harmonizes bioethics, regulatory science, and priorities in public health has the potential to bridge existing gaps among traditional and contemporary healthcare systems. Digital technologies such as blockchain and AI are able to facilitate transparency, informed consent, and compliance monitoring. Additionally, harmonized international policy is able to facilitate cross-border collaboration with accountability, equitable access, and safety. (Bodeker & Ong, 2020) Integration of such multi-dimensional systems holds the key to a promising future of global wound care improvement.

Integration of Traditional Knowledge into Regulatory Science

Upcoming regulatory frameworks should proactively incorporate tested traditional knowledge to close the gap between timeless practice and contemporary science. This entails constructing transparent guidelines for assessing traditional evidence in a manner that is sensitive to cultural context. Acknowledgment of the skill of traditional healers and participation of the same in research and policy-making is imperative. This builds confidence, safeguards indigenous knowledge, and optimizes the applicability of regulatory decisions. This integration eventually fosters more holistic and culturally more responsive health solutions. (WHO, 2013)

Development of Unified Global Ethical Guidelines

Harmonizing global bioethical norms is important to enable ethical development and commercialization of Herbo-polymeric items. Harmonized guidelines would provide uniform safeguards for vulnerable groups in various parts of the world. Such guidelines would also harmonize informed consent practices, ensuring transparency

and participant self-determination. Moreover, such guidelines must impose fair benefit-sharing consistent with international policies like the Nagoya Protocol. Such harmonization induces trust, accountability, and ethical consistency in research and industrial practices. (United Nations, 2011) It finally advocates for equitable and prudent progress in herbal-based treatments.

Use of Digital Infrastructure for Compliance and Transparency

New digital technologies such as blockchain, mobile health platforms, and artificial intelligence are strong assets to enhance compliance and transparency in regulation of Herbo-polymeric products. Blockchain offers secure, tamper-evident history of clinical trials and supply chains to provide data integrity. Mobile platforms can enable real-time monitoring and reporting, enhancing informed consent processes and follow-up on adverse events. AI enables analysis of large datasets to identify safety signals and make more effective regulatory decisions. collectively, these technologies encourage stronger ethical regulation and foster trust for the stakeholders who are involved in the production of herbal medicine. (Sharma & Singh, 2021)

Capacity Building and Education Initiatives

Investing in capacity development through focused education programs becomes crucial to enhance ethical and regulatory competence in the arena of Herbo-polymeric products. Creating specialized curricula and ethics courses designed for researchers, traditional practitioners, and regulatory staff promotes detailed awareness of compliance needs and cultural barriers. Interdisciplinary exchange programs foster collaboration and sharing of knowledge among various sectors. These initiatives together make a more educated, ethically aware workforce better qualified to promote safe and efficacious herbal treatment throughout the world.

Multistakeholder Collaboration Platforms

Building multistakeholder cooperation frameworks that bring together governments, academia, industry, NGOs, and indigenous peoples is paramount to foster inclusive policy-making. These platforms create channels for free dialogue and building trust among diverse stakeholders. By engendering collective decision-making, such avenues allow for the co-creation of rules and moral values achievable, which respect cultural and scientific values. These platforms allow for early awareness of arising challenges, which facilitates responsible innovation and sustainable development in Herbo-polymeric products.

CONCLUSION

The discovery of herbal excipients and polymers for wound healing opens up exciting therapeutic possibilities, blending the age-old traditions of herbal medicine with modern polymer science to create novel wound healing solutions. Herbal excipients rich in bioactive molecules like flavonoids, tannins, and essential oils play a vital role in wound healing by facilitating tissue regeneration, displaying anti-inflammatory, antimicrobial, and antioxidant activities. Natural and synthetic polymers are important scaffolds used to impart structural strength, ensure a moist wound bed, and allow the controlled delivery of active ingredients, thus improving the action of herbal-based products.

Herbo-polymeric systems provide distinct benefits compared with traditional wound dressings, such as biodegradability, biocompatibility, and the ability to release therapeutic agents in a targeted and sustained fashion. These combined systems can promote the rate of wound closure, minimize the risk of infection, and reduce scarring, ultimately enhancing patient outcomes. While these novel characteristics are promising, their translation from the laboratory bench to clinical use remains problematic.

Chief among such challenges are the regulatory and ethical ones that now impede commercialization and extensive clinical acceptance. Harmonized global regulatory systems for herbal excipients and polymer-based wound dressings are lacking, which leads to uneven standards of quality and safety evaluations. Inconsistency in herbal sources, extraction processes, and polymer characterization only adds to batch-to-batch variability, making it hard for quality control as well as regulatory approval. Moreover, sparse preclinical and clinical data limit setting of solid safety and efficacy profiles that are required to gain regulatory approval.

Ethical issues must also be taken into account with caution. Intellectual property rights over traditional knowledge, fair benefit-sharing with traditionally using indigenous communities and anti-biopiracy are some of the major issues which need to be addressed so that social justice and ethical accountability are not violated.

For herbal excipients and polymers to be most effective in wound healing, different experts must cooperate. All stakeholders, including regulators, scientists, industry experts and ethicists, must come together to set up quiet, clear ways to test, describe and identify materials from ethical sources. Using this method will support new ideas, enhance safety during treatments, ensure products work well and make treatments fair for all.

Generally, combined plant medicine and polymer science has great potential to restructure how wounds are being treated. If challenges related to regulations and ethics are addressed together, Herbo-polymeric wound healing systems will be valuable, lasting and successful for patients everywhere.

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