Revolutionizing Bone Regeneration: A Comprehensive Review On Bone Grafts

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Abstract: Herbal medicines are plant-based medicines and have been documented 4000 years back. Great results have been extracted from several studies with a minimum amount of side effects. These medicines help osteogenesis as the bone grafts obtained from such are utilized as a filler and scaffold. Such grafts are bioresorbable and do not possess any reaction like antigen antibodies. The aim is to have a comprehensive review study on bone grafts. This review article covers a combination of all aspects regarding bone grafts and their different forms of availability. The Objectives of this review are to explore various bone grafts and to summarize them so that the reader can have enough information just by reading this article. The article gives thorough information about bone grafts and mainly focuses on several ethnopharmacological studies collected using databases such as Pubmed, Medline, Scopus, and Google Scholar. Regarding their osteogenic, angiogenic, anti-inflammatory, and remodeling effects, acting on bone receptors, promoting bone metabolism, increasing mineral uptake, and supporting free radical oxidation, Chenopodium ambrosioides, Piper sarmentosum, Quadrangularis Cissus, Ricinus communis, and Radix salviae miltiorrhize plants were the most extensively studied in several works of literature. This article concludes that using herbal bone grafts on the site of a defect holds promise for bone regeneration and offers an alternative to conventional therapies when they are impractical. Very few studies have been conducted to date and this has raised interest in using herbal bone grafts.

Keywords: Herbal medicine plants, osteogenic, filler, scaffold, ethnopharmacological, regeneration.

Funding: This research did not receive any specific grant from any funding agencies in the public, commercial or not for profit sectors.


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INTRODUCTION

Herbal medicines are a healthier choice. Surgery, trauma, infection, or congenital malformations can all lead to ridge defects. To improve bone and soft tissue healing, osseous replacement aims to maintain contour, eliminate dead space, and decrease postoperative infection. When a tooth is lost, rapid resorption of alveolar bone is seen, for instance, in the pneumatization of the maxillary sinus after the tooth is compromised. Bone grafting is a surgical process where the missing bone is replaced with the patient's bone, artificial, synthetic, or natural bone replacements. When growing natural bone entirely replaces the graft material, a fully integrated area of new bone is created. Numerous factors, such as tissue viability, defect dimension, graft shape, dimension, volume, biomechanical qualities, graft handling, cost, ethical issues, biological characteristics, and associated consequences, might affect the selection of the best bone graft. Autografts, allografts, and xenografts are three major materials utilized in bone grafting. Other alternatives include tissue-engineered biomaterials with synthetic or biological foundations and mixtures of these biomaterials. Each of these choices offers benefits and drawbacks. Allografts and xenografts lack the osteogenic qualities of autografts but have osteoinductive and osteoconductive features. Autografts have significant osteogenic qualities that are important for bone healing, modeling, and remodeling and are known to be the golden standard for rebuilding tiny bone lesions. Discomfort, donor site complications, and extra risks, including significant artery or visceral injury during harvest, are among the disadvantages of autografts. These factors have led to introducing and testing various alternative choices. Allografts are a different option, although they have significant drawbacks such as rejection, disease transmission, and expense. Allografts have less integrating qualities with the host's recovering tissues than autografts. Moreover, the drawbacks of allografts are that xenografts risk spreading zoonotic illnesses, and graft refusal is more common and severe. The last ten years have seen the introduction of tissue engineering in response to these issues. The methodology of tissue development includes the use of appropriate scaffolds, the addition of appropriate growth stimulants and cells, and, in recent times, the use of appropriate stem cells. To lessen the limitations of traditional grafts and improve graft acceptance, osteogenicity, osteoconductivity, and osteointegration, innovative scaffolds and tissue grafts can be made utilizing tissue engineering techniques.

BIOLOGY OF BONE STRUCTURE

Before knowing about bone grafts, it is essential to know the biological configuration of bone. The bone, a hard organ in the body, may protect and support a variety of organs while also facilitating mobility. The amazing hierarchical architecture, which comprises the brittle apatite mineral and the supple collagen protein, is largely responsible for this characteristic. Regardless of understanding that the gross structures of bones of numerous kinds and species differ and the organizations of the protein collagen and minerals remain unresolved, the mineralized fibrils, which are bonded together by collagen peptides and mineralized by apatite crystals throughout the development of the bone, continue to function as the bone's common fundamental building block. The stiffness of bone tissue, which is influenced by the natural mineral content of the collagen/mineral composite, is connected to bone tissue's functioning in the human body. For instance, the ear vibrates to transmit sound with great quality since it contains over 80% minerals, yet it cannot resorb energy. Deer antlers, conversely, are not load-bearing but can distort while absorbing energy due to less dense mineral composition. Because the long bone's mineral concentration is over 20%, it can absorb energy and maintain its lightweight for movement. Once produced, the bone is actively maintained by two distinct processes, modeling and remodeling, which are also part of bone fracture healing. While bone remodeling involves the production of new bone after bone resorption, bone modeling involves the formation of new bone beforehand. During growth, there is active bone modeling that changes the size and form of the bone. By improving one's capacity to withstand bending and adjust to functional difficulties, it persists throughout adulthood. Bone remodeling is a continual process that starts before fetal development and is responsible for preserving bone function by consistently replacing the worn-out bone with new bone. According to reports, 3% of cortical and 25% of trabecular bone are eliminated and replaced annually. Except for emerging loads beyond bone potency or progressively accumulating damage under cyclic loading, the dynamic equilibrium of the bone effectively avoids bone fracture. It has been demonstrated that, in contrast to other tissues, bone healing recapitulates the ontological processes that occur all through the embryonic growth of the skeleton, enabling the wounded organ to be entirely recovered to its pre-injury formulation, structure, and function. The amount of tissue loss is one of the mending parameters that may be used to categorize bone healing.

PROPERTIES OF BONE GRAFTS

Knowledge of each graft's biological characteristics is required to choose which is best for a certain ailment. The features of a good bone graft material are osteogenensis, osteoinductivity, osteoconduction, and osseointegration. Osteogenesis is the ability of osteoblasts to differentiate osteoprogenitor cells from either the receiver's bone or generate new bone. In contrast to allografts and xenografts, which have minimal survivability following implantation of their cellular structures, autogenous grafts primarily possess this feature. By differentiating multipotent mesenchymal stem cells (MSCs) from the adjoining host tissues to create osteoprogenitor cells, later the osteoblasts are formed; osteoinduction is the capacity of the biomaterial to encourage the formation of bone cells. Growth factors such as bone morphogenetic proteins (BMPs), including BMP-2 and BMP-7, transforming growth factor- (TGF-), fibroblast growth factor (FGF), insulin-like growth factor (IGF), and platelet-derived growth factor (PDGF) have been shown to have this capability. The graft's ability to operate as a permanent, biodegradable scaffold known as osteocondution allows for the mechanical support of new bone and angiogenesis from the margins of the defect into and onto its surfaces. New bone development is started or induced by this trait. Last but not least, osseointegration is the ability of the graft to adhere to the adjacent bone without a layer of fibrous connective tissue in between, allowing for the inclusion of the graft at the place of installation. These techniques may categorize all bone grafts and materials used as bone graft substitutes. Only autografts have all of the characteristics above among all forms of bone transplants. Few characteristics out of four of...
the supreme bone graft material osseointegration, osteoconduction, and maybe osteoinduction are present in allografts and xenografts, and they lack osteogenic qualities. In certain circumstances, bone transplants are necessary to maintain the structure while encouraging bone healing. Bone grafts like cortical and vascularized bone grafts are good choices when structural support is needed.

<table>
<thead>
<tr>
<th>Table 1: Commonly used natural tissues and biomaterial grafts</th>
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<tbody>
<tr>
<td><strong>Bone replacement graft materials</strong></td>
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<tr>
<td>Human bone grafts tissues</td>
</tr>
<tr>
<td>a) Autografts</td>
</tr>
<tr>
<td>- Extra-oral</td>
</tr>
<tr>
<td>- Intra-oral</td>
</tr>
<tr>
<td>b) Allografts</td>
</tr>
<tr>
<td>- Fresh or frozen bone</td>
</tr>
<tr>
<td>- Freeze-dried bone allograft</td>
</tr>
<tr>
<td>- Demineralized freeze-dried bone allograft (DFDBA)</td>
</tr>
<tr>
<td>Non-human source materials</td>
</tr>
<tr>
<td>a) Xenografts</td>
</tr>
<tr>
<td>- Bovine hydroxyapatite</td>
</tr>
<tr>
<td>- Porcine bone</td>
</tr>
<tr>
<td>- Equine bone</td>
</tr>
<tr>
<td>- Coralline calcium carbonate</td>
</tr>
<tr>
<td>Synthetic materials (Alloplasts)</td>
</tr>
<tr>
<td>a) Bioactive glasses</td>
</tr>
<tr>
<td>b) Calcium phosphates</td>
</tr>
<tr>
<td>- Hydroxyapatite</td>
</tr>
<tr>
<td>- Tricalcium phosphate</td>
</tr>
<tr>
<td>- Other calcium phosphates (Brushite, monetite, calcium polyphosphates/CPP)</td>
</tr>
<tr>
<td>c) Calcium sulfate</td>
</tr>
</tbody>
</table>

**Fig1a. Extraction socket**

**Fig1b. Graft material placement in socket followed by extraction**
4. AUTOGRRAFTS

Autografts are those taken from one place and replaced into a different site of the same individual. They can be cortico-cancellous grafts that combine cortical and cancellous (non-vascularized or vascularized) bone types. Survivor cells and bone-building peptides are present in fresh autografts. They are the greatest material currently accessible from a biological standpoint since they have zero immunogenicity. After transplantation, they stay alive immediately, and their absence of immunogenicity enhances the possibility that the graft will be incorporated into the host site. Moreover, fresh autografts' osteogenic, osteoinductive, and osteoconductive properties are optimal because they include MSCs, osteogenic bone marrow-derived cells, and growth factors. Autografts have no associated possibility of spreading viruses in addition to providing skeletal reinforcement for surgically placed devices and eventually growing into technically efficient structures as they progressively replace nearby bone through creeping replacement. The biggest disadvantage is that autografts must be taken from a different body region, requiring further surgery and increasing the risk of discomfort, morbidity, and problems at the donor site. If extensive grafting is required, enough autograft quantities might not be available; hence other bone graft materials must be taken into account. The tissues from the grafts were harvested from a variety of locations. Possible sources for grafts include the iliac crest or other parts of the body. Each of these sources has benefits and drawbacks. In 18 patients, Kitzinger et al. compared the iliac crest and the distal radius as the sources of bone graft; they found that the distal part of the radius was a better alternative because, in their situation, it eliminated the need for general anesthesia, cut down on the length of the procedure, and required less surgical exposure. The best autografts for actual bone transplantation are cancellous or pedicled, circumscribed cortical autografts. The success of autogenic bone grafting depends on several factors, including the osteogenic cells' ability to survive and proliferate, the conditions at the site of the transplantation bed, the type of graft utilized, how it is handled, and how the graft is shaped to match the host's bone during surgery. Although a fresh autologous graft can assist the genesis, conduction, integration, and stimulation of new bone formation, a bone graft substitution might not be required to possess all the mentioned characteristics to be clinically successful naturally. If minimal concentration and dosage criteria are satisfied when formative chemicals are locally given on a scaffold, stem cells from the mesenchymal layer are eventually recruited to the area and have the potential of consistently stimulating the formation of new bone.

5. ALLOGRAFTS

The allograft can be used as a substitute for autogenous bone transplant since it may cause harvesting-related difficulties and has a cap on the amount of graft that may be taken from the patient. As the donor screening methods were developed, the risk of infection decreased. Bone allograft benefits include unrestricted material usage, no donor-site morbidity, and accessibility to mechanical support in various forms and dimensions. The most common methods for storing bone allograft are freezing and drying, and vacuum packaging. However, the drawbacks of the allograft include concerns that the structural quality of the bone may deteriorate and that sterilizing and storing it will kill any living osteogenic cells. Compared to an autogenous transplant, these mechanisms reduce the allograft's ability to mend the bone and cause a loss of osteogenic and osteoinductive activity. As a result, it is largely employed in osteoconduction by giving some mechanical support. Among the major issues with homologous bone is that there is still a risk of infection from viruses and other agents despite meticulous screening of donors and plasma samples. However, with a risk ratio of 1:1.6 million, there were barely two cases of HIV infection that were documented. Even the many sterilization techniques now in use cannot eradicate these kinds of infections. The most often employed approach in individual medical facilities is freezing or freezing-drying, which can completely reduce the possibility of viral infection. Ethylene oxide gas cannot enter the cortical bone, despite some individuals emphasizing that it can stop viral infection. Other techniques of sterilization, like irradiation, can be used. Due to the allograft's lack of osteogenesis and poor osteoinductivity, as well as the effects of sterilization and storage on osteoconductivity and osteoinductivity, the bone union rate after allograft inclusion may be low. The allogeneic bone integrates similarly to nonvascularized autogenous bone grafts. However, the period of incorporation relies on the dimensions of the allograft. This characteristic is partly explained by the absence of cells needed for bone regeneration and immune responses that develop during the incorporation of allogeneic bone in the donor location. Since it lacks structural stability, allogeneic cancellous bone is frequently used to treat incomplete bone...
defects instead of segmented or whole-bone deficiencies in clinical settings. Clinically, it is frequently employed to pack the bone defect and enhance spinal fusion, particularly in revision arthroplasty. Two well-known ossification processes are intramembranous ossification and enchondral ossification over the transplant bone’s surface. Allogeneic bone is surrounded by an exterior callus with bridging enchondral bone growth, and at the same time, cortical bone resorption and creeping replacement take place. The two bones are thus joined as though by welding. Additionally, only the junction undergoes fusion, and the innermost portion of a transplanted bone retains most of its dead bone trabecular for several years. The third to sixth month is now when bone strength is at its lowest, and the first to second year is when it gradually improves.

6. XENOGRAFTS

Xenografts, called heterologous or xenogenic grafts, are an additional option for autogenous bone transplants. One person’s xenografts are removed and implanted in another individual with different species. If xenogenous bone grafts could be treated to make them safe for transplantation in people, there would be an endless supply of material. Xenografts mend the bone defect and enhance spinal fusion, particularly in revision arthroplasty. Two well-known ossification processes are intramembranous ossification and enchondral ossification over the transplant bone’s surface. Allogeneic bone is surrounded by an exterior callus with bridging enchondral bone growth, and at the same time, cortical bone resorption and creeping replacement take place. The two bones are thus joined as though by welding. Additionally, only the junction undergoes fusion, and the innermost portion of a transplanted bone retains most of its dead bone trabecular for several years. The third to sixth month is now when bone strength is at its lowest, and the first to second year is when it gradually improves.

Fig 2: Types of bone grafts

(A) Autograft: To fill the bone deficiency, the surgeon removes the bone from one site and incorporates it into another site of the same person. (B&C) Allograft and Xenograft: The bone transplant is taken from a human giver or an animal. Xenografts risk trigger an immune reaction and spread bacterial and viral infections and zoonotic diseases. (D) Synthetic bone graft: There are several kinds of artificial grafts. These grafts are secure and do not require a second surgical site.

7. IMMUNE RESPONSES

By generating pro-inflammatory cytokines, including interleukin-2 (IL-2), interferon (IFN), and tumor necrosis factor (TNF), which activate macrophages, Th1 cells can lead to poor remodeling of tissues and refusal of each allograft and xenograft transplants. Instead of stimulating macrophages, Th2 cells produce IL-4, IL-5, IL-6, and IL-10 cytokines, which are likely related to graft integration. Macrophages can be categorized as M1 or M2 cells depending on how their receptors express, function, and release cytokines. Rat M1 macrophages express CD68 and CD80 on their surface and produce large amounts of cytokines that promote inflammation, including IL-12 and TNF. Rat M2 macrophages, on the other hand, exhibit CD16 surface markers, produce large quantities of IL-10 and TGF-β, prevent the generation of cytokines that promote inflammation, and support favorable tissue remodelling. The Th2
lymphocyte response, which is advantageous for tissue remodeling, is induced by M2 macrophages. The extracellular matrix (ECM) of the scaffold, which contains cellular material, modifies the recipient’s immune response after implantation by altering the phenotype of macrophages and lymphocytes; this might affect the result of tissue remodeling in terms of acceptance or rejection. A cellular transplant can cause connective tissue to deposit and the rejection of the graft by inducing an M1 macrophage and Th1 lymphocyte response. An acellular graft induces an M2 macrophage and Th2 lymphocyte response, which results in greater beneficial tissue remodeling and graft acceptance.

### Table 2: Advantages and Disadvantages of Some Biological and Synthetic Tissue-Engineered Polymers

<table>
<thead>
<tr>
<th>Tissue-engineered polymer</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collagen</td>
<td>Most important ECM component, high availability, simplicity of purification from live creatures, non-antigenicity, biodegradability, biocompatibility, and bioreabsorption, non-toxic biological plastic due to high tensile strength, and formulation in a variety of forms</td>
<td>Pure type I collagen is expensive, isolated type I collagen varies, hydrophilicity causes swelling and faster release, bovine spongiform encephalopathy (BSE) and mineralization are side effects, and limited cell differentiation and poor bone-forming capacity are further factors.</td>
</tr>
<tr>
<td>Chitosan</td>
<td>The material’s biocompatibility, adsorption capabilities, capacity to promote cell differentiation, encouragement of osteoblast development and separation in cell culture, porous structure, flexibility, good structural properties, and appropriateness for cell ingrowth are only a few of its qualities.</td>
<td>Low solubility, insufficient capacity to create new bone, allergic responses, and non-osteococonductive.</td>
</tr>
<tr>
<td>Alginate</td>
<td>Non-toxic; biodegradable; less costly; fast to set; simple to mix, handle, and utilise</td>
<td>Low mechanical stability (microparticles made exclusively with calcium alginate), poor dimensional stability, untidy to deal with, and less precise replication of detail</td>
</tr>
<tr>
<td>Calcium phosphate</td>
<td>Outstanding biological qualities, probable resorbability, ideal bone-implant contact, simple surgical preparation, small bone defect, full adaptation to the bone cavity, outstanding biocompatibility, bioactivity, good molding capabilities, and simple manipulation</td>
<td>Low flexural/tensile strength, brittleness, and mechanical resistance</td>
</tr>
</tbody>
</table>

### 8. ETHNOPHARMACOLOGICAL USE OF MEDICINAL PLANTS IN OSTEOINTEGRATION

The World Health Organization estimates that about 80% of the world’s population still relies on such plants as their primary source of medicines and that about 50,000 plant species have been registered for their medicinal uses. The scientific community has investigated and validated several plants that indigenous and underprivileged communities have historically used as sources of raw materials and to create new biomaterial prototypes. For human survival and well-being, as well as preserving biodiversity, forests’ ecosystem services are essential. Indigenous peoples worldwide use the forest for various purposes, including agriculture, fishing, hunting, medicine, building materials, and implements. These uses are particularly prevalent in underdeveloped areas where it is difficult to obtain traditional medicines. More than 25% of medicines available today come from medicinal plants. Although it differs between nations, the global market for herbal medicines has grown over the past ten years in tandem with pharmaceutical and clinical research. Researchers conducted ethnomedicinal studies in communities and tribes worldwide, including India, Cameroon, the Philippines, Bangladesh, Brazil, and Southeast Asia. They examined the effectiveness of using traditional medicinal plants to treat various diseases, concentrating on those that could heal bone fractures. These plants were used in various ways, including topical application as pastes and systemic application as infusions and teas, depending on the type of bone fracture. The positive effects of using herbal extracts traditionally to repair bone fractures are frequently mentioned, but there aren’t many studies to back them up. As a result, medicinal plants as complementary therapies hold promise for bone regeneration because they are biocompatible, convenient to use and store, and have been shown to promote osteogenesis. The main functions and mechanisms of the medicinal plants mentioned in the research literature concerning the process of bone repair have been listed:

#### 8.1. Dysphania ambrosioides

The Brazilian and Latin American populations have long used *Dysphania ambrosioides* (L) Mosyakin and Clemants (*syn. Chenopodium ambrosioides* L) as a traditional remedy for inflammatory conditions and treating bruises and fractures. *D. ambrosioides* acts as an important osteointegration agent, demonstrating the importance of medicinal plants in phytomedicine production.

#### 8.2. Piper sarmentosum

Southeast Asia has a *Piper Sarmentosum* (Ps) plant, typically used as a food flavoring. Its extract has been used in Malaysia to treat menstrual irregularities, coughs, and toothaches. There have been claims that various Ps plant...
extracts have anti-inflammatory, antimicrobial, antioxidant, and anticarcinogenic properties\textsuperscript{92}.

### 8.3. Cissus quadrangularis

*Cissus quadrangularis*, a perennial plant called linn, is primarily found in the world’s hottest regions, including India, Sri Lanka, tropical Africa, South Africa, Thailand, Java, and the Philippines\textsuperscript{93}. The plant treats irregular menstruation, bloody diarrhea, skin issues, earaches, and hemorrhoids. It accelerates the healing of bone fractures, as mentioned in ancient medical systems like Ayurveda. Beyond bone remineralization, plant phytoconstituents are notable and support their various therapeutic activities\textsuperscript{94}. Singh et al. evaluated osteopontin expression during treatment with *C. quadrangular* extract capsules orally in a study with patients who had mandibular fractures compared to the control group. Rats given systemic *C. quadrangular* showed complete restoration of the normal bone composition following fracture in 4 weeks as opposed to 6 weeks for controls. The period it took for bones to heal was shortened by about two weeks. Indications of quicker bone remodeling include the total weight of the fractured bone returning to normal much sooner than in controls. The treated group experienced an acceleration of all events, including fibroblastic, collagenous, and osteochondral, in 10 to 14 days\textsuperscript{95}.

### 8.4. Cannabis sativa L. (Cs)

Since ancient times, people have used *Cannabis sativa L. (Cs)* for therapeutic and recreational purposes. Its medicinal applications have been documented as far back as ancient China, medieval Persia, and 14th-century Europe. These applications include the treatment of headaches, fever, gastrointestinal issues, malaria, and even as an antibiotic. The plant contains over 100 compounds, but 11-Tetrahydrocannabinol (THC) and Cannabidiol are the two most prevalent ones (CBD). Both influence the endocannabinoid system, which all mammals have as a physiological regulator. It also possesses several therapeutic properties, including appetite stimulants, antiemetic, antitumor activity, analgesic, anti-inflammatory, anxiolytic, and anticonvulsant. However, its medicinal use is still restricted due to side effects, social stigma, and legislation\textsuperscript{96-98}.

### 8.5. Ricinus communis L.

Originally from southern Asia, the castor bean (*Ricinus communis L*) plant is now widely distributed, particularly in tropical and subtropical areas. According to reports, the plant has larvicide, antitumor, anti-implantation, anti-inflammatory, antidiabetic, central analgesic, antioxidant, anti-inflammatory, anti-implantation, anti-asthmatic, antitumor, and antitumor. These uses result from specific plant constituents being present\textsuperscript{99, 100}. Polyurethane, a polymer with excellent properties, is produced by extracting castor oil from the fruit of *R. communis*. To find biomaterials that can be used as growth promoters and molecule carriers that will aid in the healing of significant bone defects, such as grafts, many current studies in bone tissue engineering have focused on plant polymers. These polymers act as bone cement\textsuperscript{101}. Del Carlo et al. discovered that castor bean polymer stimulates osteogenesis and osteoconduction when combined with calcium, particularly when stem cells are present because they promote the movement of periocular tissues, capillaries, and osteoprogenitor cells\textsuperscript{102}.

### 8.6. Ulmus wallichiana

The South Himalayan plant *Ulmus wallichiana Planch* is a significant one used to treat bone fractures in humans and animals. Swarnkar et al. showed the effectiveness of this compound in osteoblast induction and differentiation in osteoblast cultures extracted from rat calvaria to study bone differentiation promoted by naringenin. Utilizing computed tomography to analyze the rat calvaria’s bone microarchitecture and fluorescent bone marking to identify new bone formation, the effectiveness in vivo was assessed\textsuperscript{92}.

### 8.7. Bixa Orellana L.

The native Brazilian plant *Bixa Orellana L* grows in other parts of South and Central America. Tryptophan, methionine, and lysine are the amino acids, carotenoids (bixin and norbixin), and fatty acids that make up its chemical makeup. It also contains small amounts of linoleic and oleic acid\textsuperscript{103}. Alves et al. examined the healing potential of polystyrene membrane coated with norbixin and collagen (PSNC) and photobiomodulation (PBM) laser (780 nm) in rats with calvarial bone defects. They were employed to gauge the progress of bone repair\textsuperscript{104}. Animal model studies have demonstrated that using various biomaterials, either with or without the PBM laser, increased bone consolidation\textsuperscript{105, 106}.

### 8.8. Pueraria Lobata

Traditional medicine frequently used to stop the loss of bone density is Puerariae root, also known as Ge Gen, which is derived from *Pueraria lobata* root\textsuperscript{107}. When studied in a bone defect healing model in mice, pueraria, one of the main phytoestrogens isolated from Gegen root (*Pueraria Lobata Wild*), acted as a potent osteogenic agent, proving to be safe and ideal in bone defect repair\textsuperscript{108}. *Pueraria lobata* and *Salvia miltiorrhiza* were used in a rat model study of calvarv defect that combined collagen structure and herbal extracts to show that these species accelerated osteogenesis when used separately with the collagen matrix\textsuperscript{109}.

### 8.9. Radix salviae miltiorrhizae

Another popular and well-known medicinal plant is Danshen, *Radix salviae miltiorrhizae*. Danshen has been shown in one study to increase local bone neof ormation in fractures that were experimentally induced in rabbit parietal bone, demonstrating its efficacy in promoting the healing of bone fractures. Additionally, it can be used as a bone graft, particularly in circumstances where vascular responses are compromised, enhancing the local vascular response. The *Radix salviae miltiorrhizae* plant contains salvianolic acid B (ASB), which has been described as a potent anabolic agent. So it has improved the healing of osteoporotic fractures when studied against glucocorticoid-induced osteoporosis\textsuperscript{10}. It was discovered that ASB and its analogs could boost angiogenesis, lessen bone marrow adipogenesis, and promote osteocyte and lacunar canaliculi growth. In turn, this would increase the volume of blood vessels to supply nutrition to the bone and could be used as a bone graft, especially in situations where vascular responses are compromised\textsuperscript{111}.
9. DISCUSSION

Numerous studies have demonstrated that various factors, including composition, fabrication technique, structural details at the macroscopic and microscopic levels, mechanical properties, premodification, and whether growth factors are coated on the scaffolds, affect their capacity to repair and regeneration. Plants used to treat bones must exhibit significant properties through their active constituents, exhibiting the following activities: antimicrobial; antioxidant, important in scavenging free radicals that delay bone healing; osteogenic activity, promoting increased osteoblast proliferation, osteocytes, and osteoclasts; angiogenic activity, acting on the supply of nutrients to the fracture bed, stimulating collagen production; and estrogenic activity, to control edema and pain production of chemical mediators are essential along its anti-inflammatory property. In 2014, B Santhosh Kumar and T Hemalatha conducted a study that showed that implants made up of Biphasic calcium phosphate–casein bone graft fortified with Cassia occidentalis have better mechanical and osteoinductive capabilities. Additionally, the BCP-casein-CO implant has good cytocompatibility and promotes cell growth and proliferation. The BCP-casein-CO implant’s mechanical strength is sufficient to support bone tissue engineering and regeneration. Another study was conducted on rat calvaria to assess the potential of herbal plants, carried out by Dong-Hwan Lee and Il-Kyu Kim in 2017. Histological analyses revealed that Danshen and Ge Gan extractions increased bone formation activity when used with collagen matrix in this in vivo experiment on rat calvarial bone defect. This effect most likely has angiogenesis as its mechanism. Vicente F. Pinheiro Neto and Rachel M. Ribeiro compared the use of Chenopodium ambrosioides to other bone grafts already used in surgical procedures, such as Ricinus communis (castor oil) polyurethane and autogenous bone marrow, for the osseointegration of fractures in rabbits. According to the data, the fact that C. ambrosioides graft and autogenous bone marrow have a stronger capacity to promote bone regeneration than castor oil graft indicates that the medicinal plant may have therapeutic advantages for bone tissue. Guo-Chung Dong, Huei Min Chen, Ricky W.K. Wong, and A. Bakr M. Rabie contrasted the quantity of new bone that Gusuibu in collagen grafts generated to the amount that bone and collagen grafts produced. Compared to defects transplanted with bone and collagen, defects grafted with Gusuibu had 24% and 90% more new bone, respectively. In the passive control group, no bone developed. Later they concluded that Gusuibu may be employed as a bone graft material and has the impact of increasing new bone growth locally in collagen grafts. Shivaji Kashite, RK Sharma, and Sachin Kadam found that the PCL-GO-CQ scaffold’s synergistic combination of graphene oxide and Cissus quadrangularis callus extract increased the osteoblastic differentiation, osteoconduction, and osteoinduction potential of the material, making it an excellent choice for bone regeneration and bone tissue engineering applications. The innovative PCLGO-CQ scaffolds, made utilizing a layer-by-layer technique, have great promise for in vivo bone tissue engineering and follow-up research on bone tissue regeneration. Susmata Bose, Naboneeta Sarkar, and Dishary Banerjee indicated that recent advancements in manufacturing using additives, together with the increasing clinical need for biomedical implants, were substantially responsible for the rapid adoption of specific to patient’s synthetic bone transplants. However, due to implant failure, synthetic implants have a limited lifespan and have short-term therapeutic success, necessitating revision procedures, particularly in younger patients. These above studies show that using medicinal plants in conjunction with collagen or other shows us improved bone health, hastens regeneration, and can be used as a bone graft material. Thus this all gives us a thought about studying such biomaterials and implementing them in medical practices. It initiates us to intensify the study related to various molecules available to us naturally.

10. CONCLUSION

The studies which have been conducted shown that using medicinal plants as a way to speed up bone healing is effective in promoting tissue regeneration. The traditional uses of plants brought by communities like Asia, Africa, and South America have been crucial as a foundation for research into medicinal herbs and as an immediate remedy for pain relief and bone lesion healing. As discovered by ethnopharmacological studies, the traditional use of medicinal plants has been supported by scientific research, demonstrating that these biomaterials have curative, anti-inflammatory, antioxidant, and osteogenic activities and can transmit significant signals for bone cell recruitment. Thus, medicinal plants are a valuable source of new biomaterials for medical practice. To develop regenerative therapies that enhance patient care and lower the cost of conventional treatment, it is crucial to study further various molecules made available by nature.

11. AUTHORS CONTRIBUTION STATEMENT

Sayali Raut prepared the manuscript under the guidance of Dr. Priyanka Paul Madhu and Dr. Amit Reche. All the authors read and approved the final version of the manuscript.

12. CONFLICT OF INTEREST

Conflict of interest declared none.

13. REFERENCES


RajeswarPegu A, Tamuli R. Assessment of human-wildlife conflicts in poba reserved Forest, Dhemaji District, Assam. INDIA.


Grassi LT. Chenopodium ambrosioides L. Erva de Santa Maria (amaranthaceae): estudo do potencial anti-inflamatório, antinociceptivo e cicatrizante.


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