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Exploring the concept and scope of polyherbal formulations: A comprehensive review

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Abstract
Polyherbal formulations (PHFs) are gaining popularity among modern and traditional medicine due to their advantage in combining the therapeutic properties of many plant species, which may often present increased efficacy, diminished toxicity, and reduced adverse effects. These formulations incorporate two or more herbs, where each is chosen for the pharmacological action, it represents that is complementary to those presented by the other formulation constituents. The bioactive compounds in PHFs can interact synergistically and cause increased therapeutic effects than single-herb formulations. This review conceptually, compositionally, and mechanistically discusses the concept of synergy in PHFs with comparison to single-herb formulations in terms of broader therapeutic applications, efficacy, safety, and cost-effectiveness. PHFs have been promising in wound healing, microbial infection management, and chronic diseases such as diabetes and cancer. This outcome reiterates the importance of polyherbal formulations, being valuable holistic therapy especially in diseases complex and multifactorial in origin.

Keywords: Polyherbal formulations (PHFs), pharmacological properties, antimicrobial, antifungal activity, anti-inflammatory effects, antioxidant potential, Antidiabetic

1. Introduction
Polyherbal formulations, that is, combining multiple herbal ingredients, are the cornerstones of traditional medicine in Asia and Africa [1]. The rationale behind these polyherbal formulations is the combination of different bioactive compounds, which may increase therapeutic outcomes in a holistic approach to health and wellness. These formulations use a number of plant ingredients because, in traditional belief, the combination of various herbs complements and enhances their individual therapeutic effects, reduces side effects, and increases treatment efficacy. The scope of the polyherbal formulations comprises a wide range from simple folk medicine to modern-day pharmacological research and clinical use [2]. Polyherbal preparations have been reported to reflect a wide range of biological activities, including antimicrobial, anti-inflammatory, anti-diabetic, anticancer, wound healing, as well as antioxidant properties, among others. This widely diverse therapeutic spectrum makes them a promising or alternative approach to modern pharmacological interventions, especially those chronic diseases such as diabetes, cancer, and heart diseases. In addition to these reasons, growing Antimicrobial Resistance (AMR) prevalence and a global trend towards natural and sustainable treatment make polyherbal formulations an area of high interest [3]. Such formulations are often more environment-friendly since they are locally sourced using plant resources that do not contain synthetic chemicals, as is usually the case in conventional drugs. Present research into polyherbal formulation is rapidly developing and introducing advanced methodologies, including the profiling of phytochemistry, *in vitro* and *in vivo* studies, and clinical studies to understand the mechanism and therapeutic benefits of such herbal formulations [4]. Still, important difficulties encountered today are standardization, quality control, and regulatory approval and are significant barriers for popularizing polyherbal formulation in mainstream medicine. It encompasses the concept of polyherbal formulations and gives information about their therapeutic potency, applications, mechanisms, and challenges [5]. The rationale for this book is its ambition to give a comprehensive overview and the current state of future research in the development of integrating polyherbal preparations into modern health care settings.

2. Concept of polyherbal formulations

2.1 Definition and composition

Polyherbal formulations represent medicinal products obtained from mixtures of two or more plant species according to complementarity of their therapeutic activities. They have an historical background in traditional medical practice systems, such as in Ayurveda, in Traditional Chinese Medicine, or in Siddha medicine systems. The basic principles would be to improve efficacy; reduce toxicity; and thus, have fewer side effects [6]. PHFs usually consist of different herbs that have different complementary pharmacological properties such as antimicrobial activity, or anti-inflammatory or wound healing properties. The forms which PHFs can be seen include powders, extracts, tablets, capsules, syrups, topical creams. Active constituents found in PHFs include bioactive compounds like alkaloids and flavonoids, saponins, tannin, and essential oils. These compounds are able to act on different physiological pathways, which provides broad-spectrum therapeutic effects, thereby making PHFs an important area of research in modern phytotherapy.

2.2 Mechanisms of synergism in polyherbal formulations

One of the foremost benefits of polyherbal formulations is the phenomenon known as synergism-it occurs when the combination results in effects that are together greater than the simple aggregation of individual effects [7]. It might be brought about through mechanisms:

2.2.1 Pharmacodynamic synergy: Polyherbal formulations contain active compounds from multiple herbs that target multiple biological processes and thereby reduce inflammation and modulate the immune system, leading to enhanced therapeutic outcomes.

2.2.2 Pharmacokinetic synergy: The pharmacokinetic synergy in the polyherbal formulations will ensure that the bioavailability of the active compounds, for instance, piperine from black pepper, increases curcumin's bioactivity and effectiveness [8].

2.2.3 Toxicity reduction: Polyherbal combinations can reduce the toxicity that an individual herb may possess, ensuring safer prolonged use by acting in a synergistic and complementary manner.

2.2.4 Balancing opposing effects: Herbs such as licorice balance the pro-inflammatory effects against gastrointestinal side effects, so therapeutic effect while minimizing side effects. The combination of herbs increases the effectiveness and safety of polyherbal preparations and therefore enhances therapeutic potential, reduces adverse reactions, and increases patient compliance [9].

2.3 Comparison with single-herb formulations

Compared to single-herb formulations, polyherbal formulations have several advantages, which are making them an attractive option in both traditional and modern medicine [10].

2.3.1 Broader therapeutic spectrum: Single-herb preparations are used to treat specific diseases, whereas polyherbal preparations combine multiple herbs to treat a variety of symptoms or etiologies and hence provide a holistic treatment approach for wound healing.

2.3.2 Enhanced efficacy: Polyherbal formulations containing multiple herbs have better efficacy, especially in multifactorial treatment, than the single-herb formulation that may not offer broad-spectrum efficacy for complex diseases.

2.3.3 Minimized side effects: Polyherbal preparations mix single herbs to reduce their toxicity and side effects, allowing them to be used at lower doses for maximum therapeutic effect and minimum unwanted side effects such as gastrointestinal or cardiovascular disturbances [11].

2.3.4 Cultural and traditional significance: Polyherbal formulations are the creation of centuries of traditional medical practice, whereas single-herb formulations are of very recent origin and, by default, have no historic validation.

2.3.5 Cost-effectiveness: Although polyherbal formulations are more complex and multi-ingredient, they can be more cost-effective in certain therapeutic areas because they treat multiple symptoms at the same time. With such potential benefits, however, also comes the problem that is not found with single-herb formulations: problems in standardization, the variable quality and potency of herbal constituents, and the difficulty in conceptualizing the total range of interactions between herbs [12]. But such problems have not dimmed the multiple benefits and greater therapeutic scope of polyherbal preparations as an invaluable asset to both traditional and modern practice of medicine. This figure 1 depicts a holistic assessment of a polyherbal formulation on its SGLT2 inhibitory activity as well as the antihyperglycemic effects through two closely related pathways. The *in vivo* evaluation involves conducting the test with the formulation on animal models depicted by the mouse to assess their ability to inhibit SGLT2 activity. The antihyperglycemic effect those results is subsequently analysed by viewing the bar graph, which points out significant declines in blood glucose levels. Molecular docking is run in parallel as a study to investigate the interplay between compounds in the formulation and the protein SGLT2. Using computational analysis, it reveals exactly how the molecules bind to portions of the protein SGLT2, enabling mechanistic interpretations of their action as inhibitors. Together, these studies indicate that this formulation can serve as a useful therapeutic agent in glucose regulation and diabetes management.

3. Pharmacological properties of polyherbal formulations

The importance of polyherbal formulations has been significantly increasing, with their broad spectrum of pharmacological properties providing a more holistic approach to disease treatment [14]. Polyherbal formulations are a mixture of several herbs that synergistically interact with each other to provide therapeutic effects, which in most cases surpass the capability of single-herb treatment. The following points describe the key pharmacological properties of polyherbal formulations.

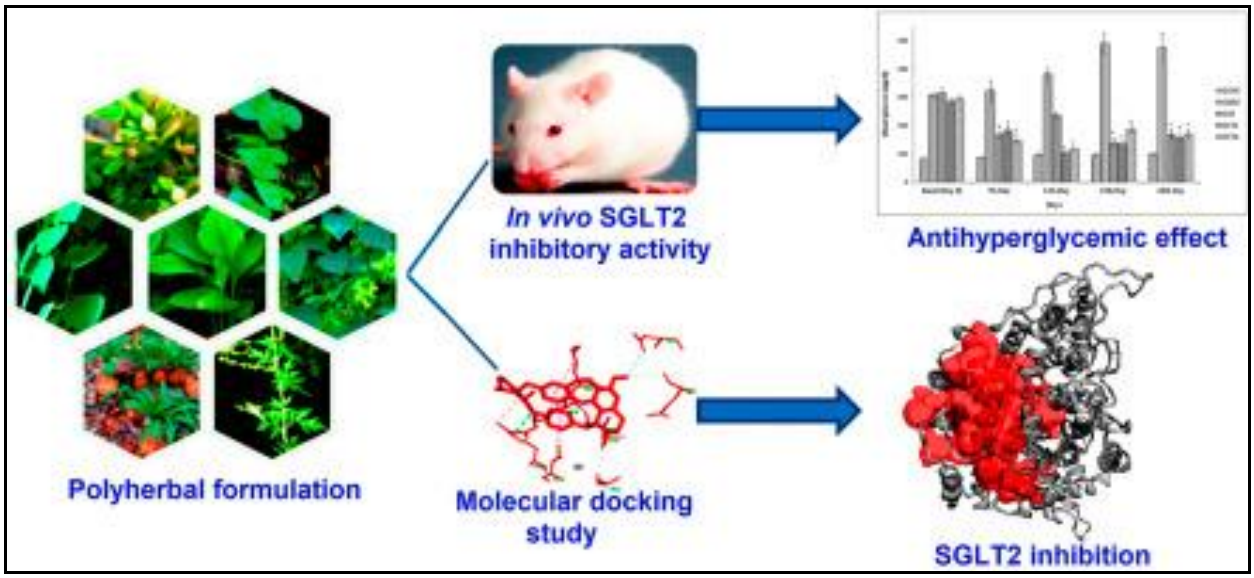

Fig 1: Polyherbal Formulations [13].

3.1 Antimicrobial and antifungal activity

These formulations show broad antimicrobial and antifungal properties. This mixture is formed using Tulsi, Neem, and Garlic. Tulsi and Neem consist of bioactive flavonoids and alkaloids with volatile oils and essential oils showing broad spectrum antimicrobial properties. They cause interference to the cell membrane of pathogens, interfere with the nucleic acid synthesis process, and protein synthesis [15]. Their interaction in such a synergistic way causes increased antimicrobial action with reduction of drug resistance against diseases that may be difficult to control by infection. This means polyherbal formulations also enhance the bioavailability of active ingredients to provide them better effectiveness in treating diseases, such as bacterial infections, skin diseases, and even fungal infections like Candida and Aspergillus species. This holistic approach in the formulation makes the use of polyherbal an attractive alternative to the more conventional antimicrobial treatment usually plagued by side effects and problems with resistance.

3.2 Anti-inflammatory effects

This group of chronic diseases is strongly contributed by inflammation; most of these include arthritis, cardiovascular diseases, and even neurodegenerative disorders. Potent anti-inflammatory properties, seen in the polyherbal formulations including Turmeric, Ginger, Boswellia, and Ashwagandha, are also useful in managing the excessive and chronic inflammatory conditions. Such bioactive compounds in the herbs inhibit pro-inflammatory enzymes as well as decrease the inflammatory cytokine's production [16]. The effect is enhanced in polyherbal formulations because multiple herbs, with their complementary mechanisms of action, target different inflammatory pathways. This synergistic interaction usually results in better outcomes by reducing inflammation and alleviating the symptoms of inflammatory diseases. For example, a polyherbal arthritis formulation could combine anti-inflammatory herbs with analgesic agents to relieve joint pain and swelling and thereby improve the quality of life of the patient. Polyherbal preparations provide multi-targeted treatment, addressing the root causes like oxidative stress or immune system dysregulation.

3.3 Antioxidant potential

Oxidative stress has emerged as a primary pathophysiological mechanism that explains many aspects of aging and different diseases, including cardiovascular disease, cancer, diabetes mellitus, and neurodegenerative disorders. Polyherbal formulations, comprising more than one herbal constituent like Amla, Green Tea, and Tulsi, contain abundant polyphenols and flavonoids along with vitamin C, thereby contributing substantial antioxidant properties [17]. They serve as free radical scavengers, protecting cells from oxidative damage. These compounds have synergistic effects, which make their formulations more potent antioxidant protection agents than single-herb preparations. Polyherbal formulations decrease cellular damage, delay the progression of chronic diseases, and promote overall health. For instance, a combination of Amla and Turmeric can protect against oxidative damage, enhance detoxification, promote liver health, and enhance immune response.

3.4 Antidiabetic and anticancer properties

Polyherbal formulations have emerged as promising formulations in the management of two of the most common chronic diseases in the world: diabetes and cancer. In diabetes, polyherbal formulations are reported to regulate blood glucose levels through enhanced insulin sensitivity, glucose uptake, and inhibition of carbohydrate digestion enzymes. Antidiabetic effects are also seen with herbs like Fenugreek, Ginseng, and Bitter Melon, which reduce blood glucose levels, decrease insulin resistance, and prevent complications from diabetes. Polyherbal formulations may work against cancer by inhibiting cancer cell growth, bringing about apoptosis, and inhibiting metastasis [18]. In Turmeric, anticancer activity was also documented, showing significant modulation in various cancer signalling pathways. The combined treatment with anticancer herbs like Garlic, Green Tea, and Ashwagandha could hit multiple cancer pathways, hence more effective as well as a holistic approach. Such effects from polyherbal formulations can synergistically increase the therapeutic benefits of herbal medicines in cancer and diabetes treatment, providing a multifaceted approach to disease management and potentially reducing side effects of conventional treatments, improving patient quality of life.

3.5 Cardioprotective and Neuroprotective effects

Polyherbal preparations show significant cardioprotective and neuroprotective action, which has led to their use in diseases

including hypertension, atherosclerosis, heart failure, neurodegenerative disease states like Alzheimer's, Parkinson's disease, among many others [19].

3.5.1 Cardioprotective effects: Garlic, Ashwagandha, and Hawthorn are known herbs that protect the cardiovascular system. They improve blood circulation, decrease cholesterol, and prevent oxidative damage. This combination in polyherbal preparations offers a holistic approach to heart health [20].

3.5.2 Neuroprotective effects: Neurodegenerative diseases are characterized by oxidative stress, inflammation, and neuronal apoptosis. The polyherbal formulation, containing herbs such as Brahmi, Ashwagandha, and Ginseng, enhances memory, cognition, and brain functions through increased neurotransmitter activity and oxidative stress reduction [21]. The synergistic interaction of neuroprotective herbs within polyherbal formulations renders them the most holistic measures in terms of prevention and management for neurodegenerative diseases [22]. These formulations target various mechanisms of aging and dysfunction within the brain, thereby slowing down disease progression through conditions like Alzheimer's and Parkinson's while enhancing life quality.

4. Materials and Methods

This review is based on the analysis of several polyherbal formulations and their applications in a range of therapeutic areas that can be drawn from the compilation of studies evaluating such formulations for their efficacy in wound care, antimicrobial activity, wound healing, and other therapeutic interventions [23]. The studies reviewed here were accessed from scholarly articles published in the period 2013-2023, wherein the research work conducted is spread across several countries and where it has been found to increase interest globally in polyherbal formulations. The data for the review was extracted from studies, which were used to look into the impact of polyherbal formulations on the antimicrobial properties, their wound healing potential, and in other medical applications like the anti-cancer, anti-inflammatory, anti-diabetic, and cardiovascular diseases treatments. Specifically, methodologies to be employed were of especial interest to researchers such as *in vitro* and *in vivo* testing, formulation development and biological standardization.

4.1 Study selection and data collection

These studies were selected based on the relevance of their therapeutic application for polyherbal formulation such as wound healing, antimicrobial activity, and other medicinal use. The studies included within this review were gathered from various academic databases and journals in order to ensure diverse range research [24]. The studies varied in their methodologies, ranging from *in vitro* antimicrobial property evaluations to *in vivo* wound healing and tissue regeneration studies. Formulation and evaluation of polyherbal compounds, especially in the context of biological standardization, were also included.

4.2 Data analysis and interpretation

Common themes and results of studies were analysed, focusing on the effectiveness of polyherbal formulations, with special attention given to comparing the various applications of the formulations in wound healing as antimicrobial agents and to their potential for treating chronic diseases like cancer, diabetes, and cardiovascular issues [25]. The data were synthesized to emphasize trends in the research field, including increased emphasis on wound care formulation and polyherbal treatment addressing more than one therapeutic need. In addition, it is worth noting the geographical distribution of research, where special attention is paid to India, the leader in this research globally.

4.3 Statistical data and country analysis

Statistical analyses on the count of articles involving publications based on polyherbal formulation, tracking of the published articles per annum from the years 2013 till 2023, reveals some trends within the variations that were quantified so as to comprehend the pattern influencing the generation of this work [26]. Data on the number of published items by country was also examined, and it was found that while India led the way with significant research output in the field of polyherbal formulations, other countries, including Malaysia, Pakistan, and the United States also made contributions, albeit not to the same extent. Thus, this analysis helped establish a global perspective of research in polyherbal formulation and indicated areas for future study.

4.4 Application analysis

The review further classified the applications of polyherbal formulations and established that the most frequent uses of polyherbal formulation are found in wound healing followed by anti-inflammatory and antimicrobial treatment. Other applications like anti-cancer, anti-diabetic, and cardiovascular therapy were also considered, giving a complete idea about the vast scope of polyherbal formulations [27]. The diversity of applications reflects the flexibility of polyherbal compounds and gives an impetus to them in modern therapeutic practices. Among the studies consulted, the general therapeutic applications of polyherbal formulations, especially their applications in wound care and microbial infection management, showed that a considerable number of studies were done, which reveals the immense scope for both traditional and contemporary medicine.

5. Data analysis

Table 1 Summary of studies on applications of polyherbal formulation Various applications of polyherbal formulations have been considered by researchers, which gives their importance in therapeutic areas. Patel considered a polyherbal wound care formulation, Herboheal, showing the antimicrobial activity against wound-infective gram-negative bacteria and treated the infections. Ponrasu found the wound healing potential of natural biocompatible polymer-based gel of polyherbal compound, showing significant impact in rapid contraction of wounds and rapid healing through re-epithelialization, which encourages application in wound care. Rajalakshmi studied AavaraiKudineer, a Siddha formulation composed of multiple herbs, concerning antimicrobial potential, by determining its broad-spectrum effectivity against pathogenic microorganisms to emphasize the value of traditional formulations in modern medicine [28]. The research work by Rajendren and Muthuirulappan presents the wound healing activity of a polyherbal Siddha formulation with the acceleration in wound closure and tissue regeneration. Ramaiah discussed formulations and evaluations of polyherbal anthelmintic tablets, exhibiting efficacy against helminths, and biological standardization importance in the matter of their safety and efficiency. These studies show collectively that polyherbal formulations are diverse in

applications ranging from antimicrobial and wound healing properties to parasitic infection treatments, thus proving that herbal-based treatments still play an important role in the current medical field.

Table 1: Summary of Research Studies on the Applications of Polyherbal Formulations [29].

References	Topic Covered	Research Study	Title
Ramaiah *et al.* (2013) [30]	Anthelmintic activity	Focused on the formulation and evaluation of polyherbal anthelmintic tablets. Showed significant effectiveness against helminths and emphasized biological standardization.	*In vitro* biological standardization, formulation and evaluation of directly compressed polyherbal anthelmintic tablets.
Rajendren and Muthuirulappan (2014) [31]	Wound healing activity	Examined the wound healing activity of a polyherbal Siddha formulation. Demonstrated significant promotion of tissue regeneration and accelerated wound closure.	Wound healing activity of a polyherbal Siddha formulation.
Rajalakshmi *et al.* (2018) [32]	Antimicrobial potential in wound care	Explored the antimicrobial potential of Siddha polyherbal formulation Aavarai Kudineer. Showed significant antimicrobial activity against pathogenic microorganisms.	Antimicrobial potential of Siddha polyherbal formulation AavaraiKudineer.
Patel *et al.* (2019) [33]	Antimicrobial activity in wound care	Investigated the antipathogenic potential of a polyherbal wound care formulation (Herboheal) against wound-infective gram-negative bacteria. Demonstrated antimicrobial properties.	Antipathogenic potential of a polyherbal wound care formulation (Herboheal) against Certain wound-infective gram-negative bacteria.
Ponrasu *et al.* (2020) [34]	Wound healing potential	Conducted an *in vivo* study to evaluate the wound healing potential of a natural biocompatible polymer-based polyherbal compound gel. Showed significant wound healing effects.	Natural biocompatible polymer-based polyherbal compound gel for rapid wound contraction and promote re-epithelialization: an *in vivo* study.

The figure 2 suggests a notable fluctuation, but within this period, the overall trend shows that between 2013 and 2016, there is an increasing trend up to 120 publications in the year 2016. This trend may reflect some form of surge in productivity or even interest in carrying out more research studies during that particular period, which may have been spurred by either funding or perhaps institutional support towards more scholarly work [35]. However, in the subsequent years, the number of publications declined to a low of 70 in 2019, and then began to recover slightly in 2020 and 2021, stabilizing at around 75-80 publications per year. The year 2022 reflected 78 publications, but 2023 increases ever so slightly to 90. Overall, the chart shows that while there has been growth in years with higher numbers, it doesn't seem entirely stable because of the fluctuations, possibly to do with shifting academic priority, external challenges like financial or global events, the COVID-19 pandemic for example, or shifting interest in research. Despite the fluctuations, the general range remains within 60-120 publications per year, indicating a relatively consistent level of scholarly output in the observed period.

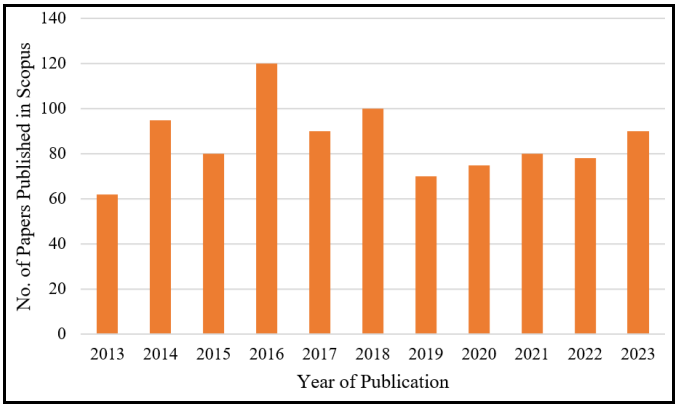

Fig 2: Trends in Publication over the Years [36].

Figure 3 illustrates the number of articles by country. With 800 articles, India features most, which shows tremendous research output differences among these nations. The leading amount published in India, according to the list, could be explained by factors such as the availability of a higher academic workforce, government drives toward increasing research, and increasing collaborative ties with the rest of the world. Malaysia, Pakistan, and the US share a moderate level of scholarly activity, with 60, 55, and 50 publications, respectively [37]. Nigeria, Saudi Arabia, Thailand, and China report significantly fewer publications, at a count of 45-30, indicating a more limited but still meaningful contribution to global scholarship. Iran and Mauritius have the lowest number of publications, 25 and 20, respectively, suggesting that their academic communities are smaller or that they may be constrained in research funding, infrastructure, or international visibility [38]. Overall, the figure suggests the disparities between countries in research output with India as a major contributor in the field, while others contribute at different levels.

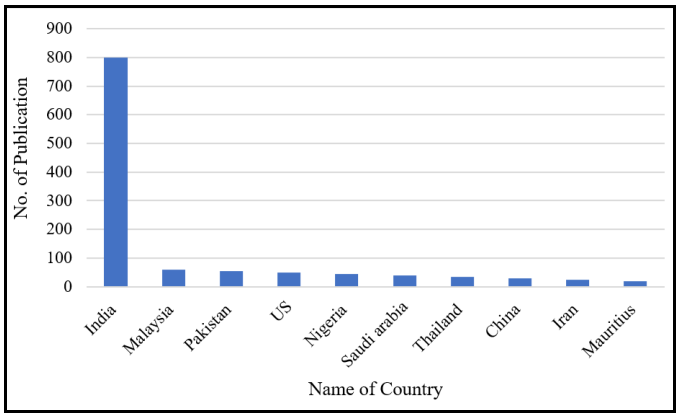

Fig 3: Publications by Country [36].

As shown in Figure 4, the percentage of wound healing agents stands out as the highest at 33%, showing that the formulations are mainly used due to their effectiveness in the wound healing process and tissue repair. The anti-inflammatory agent accounts for 19%. It is a huge part of managing inflammation, which is an underlining cause of most chronic diseases [39]. Anti-infectious agents comprise 18%, thereby indicating significant use of polyherbal formulations in controlling infections, especially microbial in

nature. Polyherbal formulations are also used as anti-cancer agents 12% and anti-diabetic agents 13% that reflects their role in the control of major diseases like cancer and diabetes. Cardiovascular disease therapy is 8% and represents their use in heart and vascular health. The "Others" category, at 5%, encompasses a range of additional uses, which would imply that polyherbal formulations have a wide spectrum of applications other than those identified above [40]. Overall, the figure suggests that the use of polyherbal formulations is very versatile, and the most prominent applications are wound healing and anti-inflammatory properties.

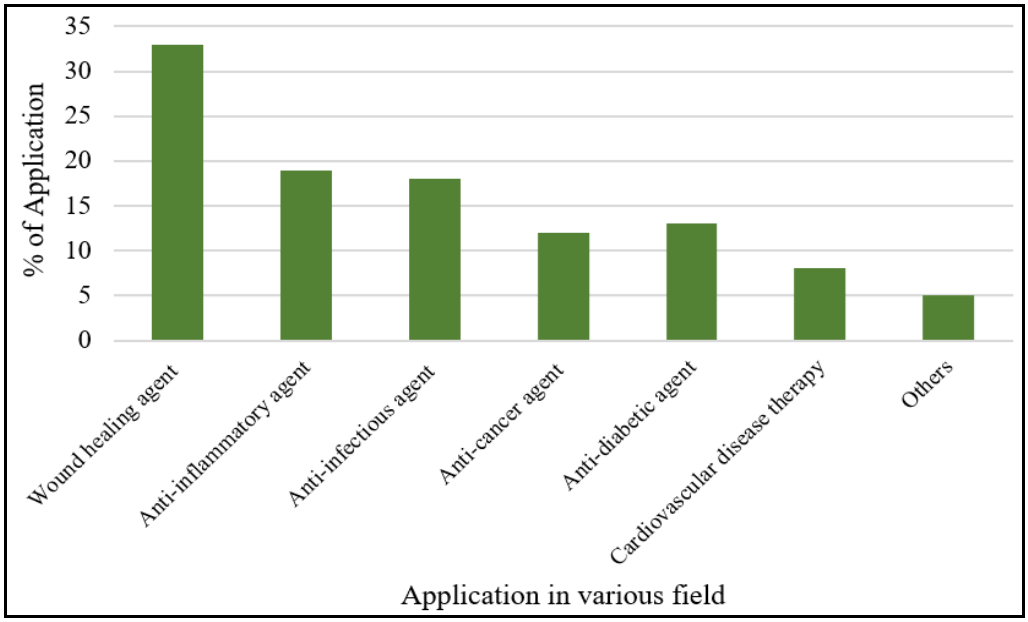

Fig 4: Percentage of Applications of Polyherbal Formulations [36].

6. Conclusion

Polyherbal formulations (PHFs) are among the modern promises and successful approaches that make use of the synergy between multiple herbs to bring more efficacy to the process with fewer adverse effects. Formulations encompass a variety of pharmacological properties: antimicrobial, anti-inflammatory, antioxidant, anticancer activities, and a comprehensive remedy for multifactorial diseases. The synergistic effects of the constituent herbs in PHFs offer enhanced therapeutic outcomes over single-herb formulations, making them a valuable alternative in both traditional and contemporary medicine. Despite standardization and complexities in interactions between herbs, the mounting research supports the potential of polyherbal formulations in the treatment of wound healing, diabetes, cancer, and cardiovascular diseases. With further research and developments, PHFs might be presented as a more comprehensive and cost-effective yet safer system of disease control worldwide.

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