POLYHERBAL FORMULATION: A PROMISING APPROACH FOR DETERMINING PHARMACOLOGICAL ACTIVITIES AND THERAPEUTIC USES

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ABSTRACT

In Ayurveda, drug definition depends on two standards: single-drug use and numerous medication use, the last option of which is known as PHF. Polypharmacy or polyherbalism is a key customary helpful natural procedure that includes consolidating a few restorative spices to increment remedial viability. The chance of polyherbalism is interested to Ayurveda despite the fact that figuring out as far as current boundaries is fascinating. The Ayurvedic composing Sarangdhar Samhita shaded the chance of polyherbal to accomplish more imperative supportive practicality. The polyherbal plan has been used commonly around the earth in view of its supportive and medicinal application. It has been seen a polyherbal treatment or zest mix. The unique phytochemical constituents of individual plants are insufficient to achieve the positive medicinal effects. The unique constituents used from the singular plants are missing to give charming pharmacological action. In articulations of pharmacokinetic synergism, the restriction of zest to work with the absorption, scattering, assimilation and, removal of various flavors is locked in. Pharmaco-elements synergism of course focuses on the synergistic effect when dynamic constituents with near supportive development are centered around a different arrangement of action. The ongoing overview wraps all of the enormous components of the polyherbal plan.

Keywords: *Polyherbal, Herbs medicine, Herbal formulation, Polyherbal therapy, Phytotherapy, PHF (Poly-herbal Formulation), polyherbal formulation, Swertia chiratia,* Curcuma longa, Pharmaco-dynamics.

INTRODUCTION

The American Diabetes Association classifies diabetes mellitus into four types. Type 1 also known as insulin dependent diabetes mellitus (IDDM) in which genetic deficiency in insulin production as a result of allergic reactions which destroy the pancreatic beta cells. Type 2 also known as non-insulin dependent diabetes mellitus (NIDDM) is combined resistance to insulin-action and insulin-secretary response. Type 3 also known as gestational diabetes causes carbohydrate intolerance with first recognition during pregnancy and type 4 (genetic defect-or medication-induced diabetes). Among all the types NIDDM accounts for approximately 90% of the diabetes cases globally. Ayurvedic system of medicine is as old as human civilization. Herbal plants produce a diverse range of bio-active molecules, making them a rich source of different types of medicines. The human body has a complex system of natural enzymatic and non-enzymatic antioxidant defenses which counteract the harmful effects of free radicals and other oxidants. Study suggest that polyherbal formulations have promising antioxidant properties in term of H_2O_2 radical scavenging activity

and validates their synergistic effect by having an improved activity in most of the formulations. As such developing a polyherbal formulation will definitely produce synergistic effect as needed comparable to standard drugs that are available in market all over the world. In the traditional system of Ayurveda, polyherbal formulations are used as drug of choice rather than individual plant extract. Chirata leaves, Haldi rhizomes, Neem seeds, Gudmar leaves, Ashwagandha stem, Gokharu fruits, Methi seeds, Jammun seeds are used in traditional medicine in the treatment of chronic cases of high blood pressure, obesity, diabetes, various digestive ailments, as well as geriatric and anti-arterioscleros is remedies. Aerobic respiration, stimulated polymer pho-nuclear leukocytes, macrophages and perioxi-somes causes formation of reactive oxygen species (ROSs). These appear to be the main endogenous sources of most of the oxidants produced by cells.

LITERATURE REVIEW

Sawarin Chumpolphant (2022) Diabetic foot ulcer (DFU) is a common and devastating complication in diabetic patients and is associated with an elevated risk of amputation and mortality. DFU remains a major therapeutic challenge due to poor understanding of its underlying pathogenesis. This complication is characterized by impaired wound healing; however, mechanisms causing this impairment are complicated and involve interactions between many different cell types and infections. In addition to other conventional DFU treatments, herbal foot baths are also common, although little is known about their mechanisms of action, and they contain a wide variety of herbal ingredients. In this study, we aimed to examine the effects of three polyherbal formulations consisting of medicinal plants used in traditional. Thai herbal foot baths on wound healing, anti-inflammation, angiogenesis, and extracellular matrix modulation using high-concentration glucose-treated human keratinocytes, in addition to antibacterial evaluation.

Prakash Raj Pandeya (2021) Obesity is a life-threatening metabolic disorder necessitating urgent development of safe and effective therapy. Currently, limited such therapeutic measures are available for obesity. The present study was designed to develop a novel, safe and effective herbal therapy for the management of obesity. A polyherbal formulation (18KHT01) was developed by homogeneously mixing a specific proportion of crude Quercus acutissima (acorn jelly powder), Camellia sinensis (dry leaf buds), and Geranium thunbergii (dry aerial part) along with Citrus limon (fruit juice). Synergistic antioxidant, antiadipogenic, and anti-obesity activities were evaluated by in vitro as well as in vivo studies. In vitro experiments revealed strong synergistic antioxidant and anti-adipogenic activities of 18KHT01. Molecular assessment of 18KHT01 showed significant down-regulation of vital adipogenic factors such as PPARγ, C/EBPα, aP2, SREBP-1c, FAS, and LPL.

P. Joshi (2020) The medicinal plants possessing antioxidant and anti-inflammatory properties are used since ancient times for curing several healthcare issues. The present study was done for evaluation of anti-oxidant and anti-inflammatory activities of Boswellia serrata, Commiphora wightii, Hemidesmus indicus, Aloe barbadensis, Withania somnifera, Zingiber officinale, Berberis

aristata, Cucurma longa and their polyherbal formulation (vati). Antioxidant activities (anion superoxide and hydrogen peroxide) were estimated using E. coli, the DNA of lymphocytes, RAW264.7 cell lines were used for estimation of anti-inflammatory activities. Various methods such as DPPH, ABTS, Superoxide method, Nitric Oxide reduction method, different protein assays and cell culture were done for the evaluation of anti-inflammatory as well as antioxidant activity. Polyherbal formulation exhibited highest DPPH and ABTS scavenging (96%) Almost all the plant extracts, as well as polyherbal formulation, were recorded to inhibit LPS-induced TNF-α production by imDC in a dose-dependent manner.

Rajalakshmi Ramamoorthy (2019) Since ancient times, medicinal plants have been widely used against dreadful pathogens due to their ability to kill microbes. Also, the limitations of the present treatment methods have led the researchers to explore for new formulations with aspects of better wound healing and control of infections. In the present study antimicrobial, antioxidant and cytotoxicity properties of a polyherbal formulation prepared from the barks of three medicinal plants for treating wound infection were investigated. The polyherbal formulation was tested for broad spectrum antimicrobial activity against gram-positive bacteria Methicillin-Resistant Staphylococcus aureus (MRSA) and gram-negative bacteria such as Pseudomonas aeruginosa, Escherichia coli, Salmonella typhi and antifungal activity against Fluconazole resistant Candida albicans.

HARIKESH MAURYA (2019) The study was designed as formulation, standardization, and evaluation of polyherbal dispersible tablet prepared for the management of kidney disorders. Dispersible tablets were prepared using aqueous root extract powder of the selected plant viz. A. officinalis, B. diffusa, C. papaya, C. fistula, C. intybus, F. hispida, F. indica, C. nurvala, S. virgaurea, and V. negundo with the help of super disintegrant addition technique using crospovidone, sodium starch glycolate and croscarmellose sodium in different percentage. Evaluation assessments such as the substantial test, weight variation, hardness, friability, content uniformity, disintegration, in vitro dispersion, stability study and IR compatibility were carried out. Micro-meritics of extracts powder were determined for all formulation, which signifying good flow properties. The substantial examination was established, which comply with official requirements for uniformity test, and the drug content was close to 100% in all formulations.

Medicines from the Past

Since ancient times, people have utilized normal items, like plants, creatures, microorganisms, and marine creatures, in meds to reduce and treat infections. As indicated by fossil records, the human utilization of plants as prescriptions might be followed back somewhere around 60,000 years. The utilization of normal items as meds must have introduced an enormous test to right on time people. Plants will keep on being a source of new helpful specialists however, because of their unregulated status, questionable viability, and possible poisonousness, the gamble/ benefit proportion of herbals is negative also, their utilization as prescriptions ought to be discouraged. The acts of most cultivators and conventional healers are based on custom. They have little commonality with clinical writing and they may, justifiably, dislike the

interruption of ordinary medication into their space.

Formulation with multiple herbs

First and foremost, PHFs are known to communicate high viability in countless illnesses. As previously mentioned, the restorative impact of homegrown med is applied because of the presence of various phytoconstituents and the impacts are additionally potentiated when viable herbals are formed together in PHFs. Cultivators treat many circumstances like asthma, dermatitis, premenstrual disorder, rheumatoid joint pain, headache, menopausal side effects, persistent exhaustion, and touchy entrail condition, among others. Natural arrangements are ideal for taken under the direction of a prepared proficient.

Plants as a Form of Medicine

Since then, there has been growing interest in science thanks to legendary descriptions of plants' curative powers. Numerous studies have demonstrated that ayurvedic medicines may speed up the healing process after an accident. Many studies have looked at the effectiveness of using medicinal herbs for treating wounds. Many types of herbal plants have been demonstrated to aid in the body's innate capacity to heal wounds. Herbal medicines may be useful for cleaning, debriding, and moisturising a wound and its surrounding region. Because they aid in blood coagulation, fight infection, and speed up the overall healing process, medicinal herbs may shorten the amount of time it takes for wounds to heal.

The World Health Organisation has approved several herbal treatments.

To establish criteria and fundamental concepts to guide future investigations on the effectiveness of herbal medicines, the WHO Regional Office for the Western Pacific established an expert committee in 1992. Many people all around the world rely on herbal remedies for prevention, repair, and enhancement of their health, and the article notes that "a few herbal medicines have withstood scientific testing." Even if many herbal remedies have not been verified as effective by contemporary research, this does not lessen the validity of traditional wisdom. In light of the fact that most currently used herbal medicines lack evidence produced by standard scientific methods to answer questions of safety and efficacy, it is necessary to develop criteria for further appropriate scientific studies of these products in order to support the rational use and further development of herbal medicines.

RESEARCH METHODOLOGY

The current literature review adapts the review method given by Webster and Watson, 2002 called concept driven systematic review approach. This review method examines the literature from the concept perspective of various authors. It is different from an author-driven approach that exclusively looks into the analysis of individual authors for multiple concepts in study. As the literature on polyherbal formulation is vast and extensive, the former method is suitable for review in the current topic. In recent times, the popularity of polyherbal formulations has drawn the attention of various researchers on this topic, thus polyherbalism seems to be a major emerging area in alternative medicine. This was undertaken to identify major themes under the research topic in terms of the application of the polyherbal formulations as mentioned in the papers. Therefore this method of review helps capture the related studies in an easy and

concise manner. However, essentially every article that was located in the Science Direct and PubMed databases was also available in the Scopus database. For this reason, the SCOPUS database was selected as the source for gathering primary data for the review.

RESULTS

Data Analysis and Optimization of Formula

MLRA and ANOVA were carried out to establish a relationship between the three independent variables (X1, X2, and X3) and one dependent variable (Y1) in the BBD. The results of MLRA (the value of the correlation coefficient and the values of coefficients) and ANOVA (Fisher's ratio and P values) are summarized in Table 2 for the chosen response (Y1).

Table 1: Observed response for the selected independent variable in box Behnken design

Group	Coded Factor			Actual value (mg/kg p.o)			Urinary oxalate (mg/dl)
	X1	X2	X3	*Tribulus terrestris*	*Bryophyllum pinnatu*	*Cyperus rotundus*	
1	1	0	–1	75	100	25	0.1073
2	0	–1	1	50	50	45	0.1292
3	–1	–1	0	25	50	35	0.1043
4	0	1	–1	50	150	25	0.1357
5	0	0	0	50	100	35	0.0842
6	1	0	1	75	100	45	0.0948
7	1	1	0	75	150	35	0.1127
8	0	–1	–1	50	50	25	0.1143
9	–1	0	–1	25	100	25	0.0782
10	–1	0	1	25	100	45	0.1247
11	–1	1	0	25	150	35	0.1253
12	1	–1	0	75	50	35	0.1058
13	0	1	1	50	150	45	0.1292

Table 2: Analysis of variance for the response Y1

Source	Urinary oxalate (Y_1)	
	F-value	*P*-value
Model	12.34	0.0313 (significant)
X_1	0.53	0.5198
X_2	9.07	0.0571
X_3	6.71	0.0810

X_1X_2	1.48	0.3102
X_1X_3	25.99	0.0146 (s)
X_2X_3	3.42	0.1616
X_1^2	0.067	0.8131
X_2^2	49.16	0.0060 (s)
X^2	17.61	0.0247 (s)
"S" indicates significant		

main effect X_1 can be considered to have a significant effect on Y1 since the two-way interaction term X_1X_3 is significant. Thus, it can be concluded that the herbal extract of TT influences the performance of CR. Model reduction (i.e., omission of some terms in the equation) is necessary since the insignificant terms are more as compared to the significant terms.

Table 3: Effect of methanolic extract of TT: BP: CR on serum parameters of control and experimental animals

Parameters		
Experimental groups	**Calcium (mg/dl)**	**Magnesium (mEq/L)**
Normal Control (NC)	7.33± 1.42	3.16±0.38
Model Control (MC)	10.09 ±0.25 #	1.08±0.07 #
Standard Control (SC)	7.99± 0.22*	10.2±0.14 *
T1	8.60± 0.05*	4.14±0.04 *
T2	8.80± 0.06*	4.007±0.03 *
T3	8.47± 0.05*	4.26±0.02 *
T4	8.50± 0.06*	3.77±0.57 *
T5	8.82± 0.06*	3.96±0.26 *
T6	8.64± 0.06*	3.97±0.27 *
T7	8.96± 0.06*	4.53±0.04 *
T8	7.61± 0.06*	6.75±0.05 *
T9	9.13± 0.07*	4.02±0.03 *
T10	7.51± 0.08*	7.70±0.05 *
T11	9.23± 0.07*	4.39±0.03 *
T12	8.97± 0.04*	4.65±0.04 *
T13	7.67± 0.06*	7.99±0.05 *

The values were expressed as mean±SEM (n=6). The statistical analysis was carried out by one-way analysis of variance (ANOVA) followed by Dunnett's Post Hoc test. P<0.05 were considered significant.# Significantly different from the Normal control group at P<0.05. *Significantly different from the Model control group at P<0.05.

Table 4: Effect of methanolic extract of TT: BP: CR on Kidney Homogenate of control and experimental animals

		Parameters		
Experimental groups	**Oxalate (mg/dl)**	**Uric acid (mg/dl)**	**Catalase (mmol)**	**Protein**
Normal	0.05±0	2.	3.01±0	3.01

control (NC)	.002	58 ±0 .1 24	.10	±0.1 0
Model control (MC)	0.85±0 .37#	5.43±0. 25ns	0.77 ±0.2 3ns	0.7 7±0 .23 #
Standard control (SC)	0.06±0 .002*	10.2±0. 14*	10.2 ±0.1 4*	10. 2±0 .14 *
T1	0.08±0 .003*	4.14±0. 045*	4.14 ±0.0 4*	4.1 4±0 .04 *
T2	0.07±0 .002*	4.007±0 .03*	4.00 7±0. 03*	4.0 07± 0.0 3*
T3	0.08±0 .002*	4.26±0. 028*	4.26 ±0.0 2*	4.2 6±0 .02 *
T4	0.07±0 .003*	3.77±0. 57*	3.77 ±0.5 7*	3.7 7±0 .57 *
T5	0.08±0 .001*	3.96±0. 26*	3.96 ±0.2 6*	3.9 6±0 .26 *
T6	0.09±0 .002*	3.97±0. 27*	3.97 ±0.2 7*	3.9 7±0 .27 *
T7	0.08±0 .001*	4.53±0. 04*	4.53 ±0.0 4*	4.5 3±0 .04 *
T8	0.07±0 .001*	6.75±0. 05*	6.75 ±0.0	6.7 5±0
			5*	.05 *
T9	0.08±0 .003*	4.02±0. 03*	4.02 ±0.0 3*	4.0 2±0 .03 *
T10	0.07±0 .002*	7.70±0. 05*	7.70 ±0.0 5*	7.7 0±0 .05 *
T11	0.08±0 .002*	4.39±0. 03*	4.39 ±0.0 3*	4.3 9±0 .03 *
T12	0.09±0 .003*	4.65±0. 05*	4.65 ±0.0 4*	4.6 5±0 .04 *
T13	0.07±0 .002*	7.99±0. 05*	7.99 ±0.0 5*	7.9 9±0 .05 *

The values were expressed as mean±SEM (n=6). The statistical analysis was carried out by one-way analysis of variance (ANOVA) followed by Dunnett's Post Hoc test. $P<0.05$ were considered significant. # Significantly different from Normal control group at $P<0.05$. *Significantly different from the Model control group at $P<0.05$. Ns indicates non-significant

CONCLUSION

Regardless of the way that polyherbal itemizing is for the most part used in many bits of the world, in any case, the logical verification is at this point lacking. Various local medicines are yet under in-vivo evaluation and have not been surveyed by clinical starters. Moreover, prosperity appraisals, for instance, toxicological examinations have not been performed. Here is a need of time to

survey polyherbal enumerating using logical procedures like clinical starter, possible bioactive blends, and frameworks of movement for the future world. Ethnopharmacology is the investigation of customary restorative purposes of plants. The wellbeing sciences are acquiring support from a developing measure of overall examination and clinical information. Substance science, luck, synthetic amalgamation, blend science, genomics, and different strategies are just a portion of the many instruments researchers utilize to find novel prescriptions. A genuine converse pharmacology procedure, where consideration is moved from centers to labs, is conceivable with a trial premise and a grip of ethnopharmacology. The cycle's prosperity depended vigorously on, yet depends on, the way that it represents no huge dangers. New, more secure, more savvy and more fruitful medicines might be found by consolidating customary thinking, contemporary medication, and present day science utilizing a frameworks approach (the "brilliant triangle"). Early phytochemical examinations of CEPE showed that notwithstanding flavonoids, alkaloids, tannins, steroids, glycosides, and phenols, the plant likewise contained proteins and starches.

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