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A Review on Therapeutic Potential of Polyherbal Formulations

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ABSTRACT

Nature has been a source of medicinal agents for more than thousands of years and herbal therapy predominates in traditional systems of medicine as well as in alternative medicine practiced in various cultures such as Indian system of medicine, Chinese Traditional Medicine, Unani classical literature. The present review deals with various polyherbal formulations used by different countries of the world. Information on traditional herbal formulations was documented in the form of research and review articles in various journals. The aim of this review is to summarize the different types of herbs used for the preparation of polyherbal formulations, their therapeutic potentials including clinical and preclinical results along with their safety and efficacy. This review will facilitate to gain all about the past scientific research and the necessary information about the enormous pharmacological activities of polyherbal formulations which will insist the young researchers for future research to protect human beings from various types of diseases and may serves as a natural gold for the promotion of mankind.

Keywords: Polyherbal, HK-07, Chooranam, Rumalaya Forte, Thapring.

INTRODUCTION

Herbal products are of interest to many patients and health care practitioners because more than 70% of World's population is rely on herbal medicines for part of their primary health care system. In different regions and cultures, herbal products are used as single herb, combination of herbs, or combination of herb(s) and drug(s). Due to several side effects of allopathic medicine, in recent years there has been an increase in the use of herbal medicine by the majority of population throughout the World.

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Polyherbal formulations with various active principles and properties have been used from ancient days to treat a wide range of human diseases. Polyherbal formulations are collection of therapeutic entities that are formulated and prepared on the basis of the healing properties of individual ingredients with respect to the condition of sickness. Such herbal constituents with diverse pharmacological activities principally work together in a dynamic way to produce maximum therapeutic benefits with minimum side effects. Nevertheless, these traditional medicinal preparations gradually lost their popularity and foothold among people due to the fast therapeutic action of allopathic system of medicine. In recent years however, renewed interest has grown on traditional herbal remedies because of many side effects observed by using synthetic drugs in allopathic medicine. At the same

time, WHO also recommends further research on traditional system of medicine. [1]

Currently, polyherbal formulations are employed for the treatment of various types of diseases, such as respiratory diseases, cancer, acquired immunodeficiency syndrome (AIDS), diabetis and ulcer in order to achieve enhanced therapeutic effects. In the present review we have included different types of polyherbal formulations used for the treatment of respiratory diseases along with other activities like immunomodulatory effects, anti-inflammatory, antipyretic, anti-microbial, antioxidant, antidepressant, CNS depressant, diuretic, myocardial infarction, anti-cancer, anti-HIV and toxicity study also.

Therapeutic Potential of Polyherbal Formulations

Polyherbal formulation having Antiasthmatic activity: A polyherbal formulation (PHE) was prepared by using ethanolic extract of *Adhatoda vasica*, *Clerodendrum serratum*, *Curcuma longa*, *Solanum xanthocarpum* and *Piper longum* in the proportion of 40%, 30%, 10%, 10% and 10%, respectively by Gohil et al. The mast cell stabilizing and anti-anaphylactic property of this PHE was investigated against compound 48/80-induced mast cell degranulation as well as triple antigen-induced anaphylaxis in rats. The polyherbal formulation produced significant reduction in the mortality of rats subjected to triple antigen-induced anaphylactical shock. It also depicted marked protection of rat mesenteric mast cells from disruption by compound 48/80 in dose dependant manner. Their study suggested anti-anaphylactic and mast cell stabilizing properties of the polyherbal formulation. [2]

HK-07 is a polyherbal formulation containing mainly the extracts of *Curcuma longa*, *Zingiber officinale*, *Piper longum*, *Emblica officinalis*, *Terminalia belerica*, *Ocimum sanctum*, *Adhatoda vasica* and *Cyperus rotundus* was prepared by Gopumadhavan *et al*. The antianaphylactic activity of HK-07 was investigated in rats using the active anaphylaxis model. The effect on mast cell stabilization was performed by *ex-vivo* challenge of antigen in sensitized rat intestinal mesenteries. Antihistaminic activity was studied in guinea pigs using histamine-induced bronchospasm where preconvulsive dyspnea was used as an end point following exposure to histamine aerosol. Dose response studies of HK-07 were conducted at 125, 250, and 500 mg/kg, *p.o.* in anaphylactic shock-induced bronchospasm in rats. The optimal dose level was used for the remaining experimental models. Treatment with HK-07 at different test concentrations showed significant reduction in signs and severity of symptoms (P<0.05), onset (P<0.001) and mortality rate (P<0.05) following anaphylactic shock-induced bronchospasm. HK-07 also significantly reduced the serum IgE levels (P<0.001) in animals compared to untreated controls. Treatment of sensitized animals with HK-07 at 500 mg/kg, *p.o.* for 2 weeks resulted in a significant reduction in the number of disrupted mast cells (P<0.001) when challenged with an antigen (horse serum). HK-07 significantly prolonged the latent period of convulsion (P<0.008) as compared to control following exposure of guinea pigs to histamine aerosol. [3]

Bharangyadi is a polyherbal compound having *Clerodendrum serratum*, *Hedychium spicatum* and *Inula racemosa* as an ingredient herbs. Evaluation of the anti-asthmatic activity of Bharangyadi through various *in-vitro* and *in-vivo* experimental models was carried out by Divya Kajaria *et al*. The results demonstrate that Bharangyadi has potent histamine antagonism property with significant mast cell stabilizing and spasmolytic activity in the experimental animals. Ethanolic extract of Bharangyadi at the doses 500 and 1000µg/ml protected from compound 48/80-evoked degranulation in dose dependent manner. Pre-treatment with Bharangyadi extract showed 80% and 86% protection from histamine induced bronchoconstriction in guinea pigs with 27.8% and 36.1% increase in preconvulsion time (equal to standard drug). Screening of Histamine antagonism activity on guinea pig ileum showed that Bharangyadi reduces the smooth muscle contraction in dose dependent manner. Increasing concentration of Bharangyadi extract with maximum dose of histamine (1.6µg) showed maximum inhibition at the dose of 50 mg (99.78%). [4]

A combination of three traditional Chinese medicinal herbs was used to prepare an anti-asthma polyherbal formulation known as ASHMITM by Bolleddula *et al*. They designed a study to determine if the anti-inflammatory effects of individual herbal constituents of ASHMITM exhibited synergy. Effects of ASHMI and its components aqueous extracts of *Ganoderma lucidum*, *Sophora flavescens* and *Glycyrrhiza uralensis*, on Th2 cytokine secretion by murine memory Th2 cells (D10.G4.1) and eotaxin-1 secretion by human lung fibroblast (HLF-1) cells were determined by measuring levels in culture supernatants by enzyme linked immunosorbent assay. Potential synergistic effects were determined by computing interaction indices from concentration-effect curve parameters. Individual herbal extracts and ASHMI (the combination of individual extracts) inhibited production of interleukin (IL)-4 and IL-5 by murine memory Th2 cells and eotaxin-1 production by HLF-1 cells. Their study showed that ASHMI is significantly more potent than any of its constituent herbs in direct suppression of IL-4 and IL-5 production by Th2 cells (no overlap in the 95% confidence intervals for IC_{25} or IC_{50}) and this is due to synergism among the ASHMI constituents. Thus ASHMI has demonstrated efficacy in both mouse models of allergic asthma and a double-blind placebo-controlled clinical trial in patients with asthma. [5]

A polyherbal formula containing *Picrorrhiza kurroa*, *Picrorrhiza kurroa* and *Zingiber officinale* was prepared and screened against asthma by Thomas *et al*. A crossover, randomized control study with this combined formula and a standardized extract of *Ginkgo*

biloba were investigated on therapy-refractory asthmatic patients. No significant improvements in asthma symptoms, pulmonary function test (PFT) and quality of life could be seen. [6]

A polyherbal formulation contains different types of herbs such as *Astragalus mongholius*, *Cordyceps sinensis*, *Radix stemonae*, *Bulbus fritillariae* and *Radix scutellariae* was prepared by Wong et al. A randomized, double-blind, placebo-controlled trial of this herbal therapy for children with asthma performed in pediatric asthma patients for six months. The results of the study showed no improvement in lung function tests and other biometrical parameters. [7]

Thuthuvalayathy Chooranam is a polyherbal formulation contains *Solanum trilobatum*, *Aristolochia indica*, *Alpinia officinarum*, *Nigella sativa*, *Madhuca lonifolia*, *Zingiber officinale*, *Piper nigrum*, *Piper longum*, *Terminalia chebula*, *Ferula asafetida* and *Piper longum*. Evaluation of safety of the Thuthuvalayathy Chooranam through acute and sub acute toxicity study was carried out by Nalini *et al*. In an acute toxicity study the drug was administered orally at a dose 2700 mg/kg *p.o.* and the animals were observed for any toxic symptoms up to 72 hours. The results indicated that there were no toxic symptoms up to the dose level of 2700 mg/kg *p.o.* In case of sub acute toxicity study Thuthuvalayathy Chooranam was tested at a dose ranging from 270 mg/kg, 1,350 mg/kg and 2700 mg/kg *p.o.* once daily for 30 days. The animals were sacrificed on 31st day. The liver, heart, lung, stomach and kidney were processed for histopathological study. The result of the sub acute toxicity study did not show evidence of any changes in body weight, food and water intake when compared with the control animals. The study revealed that Thuthuvalayathy chooranam formulation at different doses of 270, 1350, 2700 mg/kg did not show toxic effects in the animal's tissues and it was safe when administered to bronchial asthma patients. [8]

An herbal compound formulation Pentapala-04 prepared from five medicinal plants namely, *Adhatoda vasica*, *Ocimum sanctum*, *Coleus aromaticus*, *Glycyrrhiza glabra* and *Alpiania galangal*. The effect of "Pentapala-04" on ova albumin and aluminium hydroxide induced lung damage in albino wistar rats was investigated. The rats were divided into three groups of four animals each. Group I, II and III serves as control, toxic and post treatment group respectively. The results showed that there was increased level of lipid peroxidation and decreased level of antioxidants in toxic group animals. But the levels of antioxidant enzymes were restored in post treated groups of animals, which might be due to the ability of Pentapala-04 to scavenge the reactive oxygen species. Thus they demonstrated that 'pentapala-04' prevents ova albumin and aluminum hydroxide induced oxidative stress, lung injury and inflammatory changes and can be used as an antiasthmatic drug. [9]

Polyherbal formulation having Anti-arthritic Activity:

Anthronav is a polyherbal tablet formulation, contains *Yogaraj guggul*, *Simhanad guggul*, *Methi*, *Nirgundi*, *Chopchini* and *Pippali*. A study was conducted by Ashok et al to investigate antiarthritic activity of Anthronav by protein denaturation method. Aqueous extract of Anthronav at different concentrations was incubated with fresh egg albumin and bovine albumin in controlled experimental conditions and subjected to determination of absorbance. Diclofenac sodium was used as the reference drug. Anthronav possesses marked *in vitro* antiarthritic effect against the denaturation of protein. [10]

Dazzle ointment is a polyherbal formulation, used for the treatment of inflammation and rheumatoid arthritis. A study was planned to evaluate efficacy of Dazzle ointment using complete Freund's adjuvant-induced arthritic model by Hardik *et al*. It was observed that Dazzle ointment produced significant anti-arthritic effect on 21st day. In CFA treated group, there was marked increase in the ESR and WBC count which was significantly decreased by test drug Dazzle ointment and standard drug Diclofenac gel (Omni gel). The results indicate that Dazzle ointment possesses anti-arthritic activity in the experimental animal model. [11]

TLPL/AY/03/2008 is an Ayurvedic proprietary polyherbal formulation, developed and manufactured by Tulip Lab Private Limited, India in capsule dosage form. The drug is approved by Food and Drug Administration, State of Maharashtra, India. It contains *Boswellia serrata*, *Commiphora mukul*, *Withania somnifera*, *Vitex negundo*, *Ricinus communis*, *Nyctanthes arbortristis* and *Zingiber officinale*. A study was assessed by Sanjay et al, to determine the efficacy and safety of this polyherbal formulation on knee joint pain assessed on visual analogue scale (VAS) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). It was an open label, single center, prospective, clinical study conducted in 36 patients of OA Knee. Two capsules of 'TLPL/AY/03/2008' were given to all the patients twice daily orally after meals for 180 days. The mean joint pain (as assessed on VAS) reduced significantly (59.85%) and the mean WOMAC combined score, WOMAC pain sub-score, WOMAC stiffness sub-score and WOMAC difficulty sub-score also reduced significantly at the end of the study. The study provides good evidence in support of the efficacy and safety of the 'TLPL/AY/03/2008' in osteoarthritis of knee. [12]

Sub chronic toxicity studies of Asena, a poly-herbal formulation for the treatment of arthritis in Ghana, was carried out in rat by Kofi et al. In the sub chronic studies, rats were administered with Asena at 60, 600 and 1200 mg/kg daily for six weeks. Urinalysis, hematological and biochemical analyses were carried out on urine, blood and serum samples collected at the end of the six weeks treatment. Histological analysis of the liver, heart, kidney and lung tissues were also done

at the end of the treatment period. The results showed that, there were no significant differences (P<0.05) in the urinalysis and biochemical analyses in Asena treated animals compared to controls over the treatment period. Similarly, the administration of Asena to experimental rats did not adversely affect hematological indices assayed except platelets which were significantly elevated (P>0.05) in the treatment groups compared to controls. There was no noticeable morphological change in liver, kidney, lung and heart micrographs of Asena-treated and control animals. Thus the study showed that prolonged administration of Asena may not affect the normal growth nor cause organ specific toxicity in the rat. [13]

Rumalaya Forte (RF), a polyherbal formulation containing extracts of *Boswellia serrata*, *Alpinia galanga*, *Commiphora wightii*, *Glycyrrhiza glabra*, *Tinospora cordifolia* and *Tribulus terrestris* was evaluated by *in-vivo* Complete Freund's Adjuvant induced arthritis animal model in rats by Subash et al. RF 80 mg/kg and 160 mg/kg offered significant anti-inflammatory activity by inhibiting primary lesion on day 5, RF 160 mg/kg body weight has profound anti-arthritic activity than low dose RF 80 mg/kg with significant reduction in mononuclear infiltration, pannus formation and bone erosion was observed in histological studies. Dexamethasone as standard exhibited a greater reduction in body weight compared to other groups while arthritic score was comparably significant with that of RF 160 mg/kg concentration. Rumalaya forte exhibited significant anti-arthritic activity on complete Freund's adjuvant induced arthritis model in rats. Rumalaya forte both high (160 mg/kg b. wt.) and low dose (80 mg/kg b. wt.) showed significant anti-inflammatory activity. Whereas high dose showed profound anti-arthritic activity, than low dose which explains a dose dependent action of Rumalaya forte. [14]

Polyherbal formulation used in treatment of Cough and Cold: A study was conducted on traditional Chinese medicine (TCM), Baoji Tablets, which is designed to treat the common cold with summer-heat and dampness syndrome (CCSDS) by Rui-zhi *et al*. The trial is evaluated both the efficacy and safety of Baoji Tablets. The study is designed as a multicenter, phase II, parallel-group, double-blind, double-dummy, randomized and placebo-controlled trial. A total of 288 patients were recruited from four centers. The new tablets groups are administered Baoji Tablets 0.9 g and dummy Baoji Pills 3.7 g. The old pills group is administered dummy Baoji Tablets 0.9 g and Baoji Pills 3.7 g. The placebo control groups are administered dummy Baoji Tablets 0.9 g and dummy Baoji Pills 3.7 g. All the drugs are taken three times daily for 3 days. The study established the basis for a scientific and objective assessment of the efficacy and safety of Baoji Tablets for treating CCSDS and provides evidence for a phase III clinical trial. [15]

Joshanda a polyherbal formulation comprises of seven ingredients such as *Althea officinalis*, *Cordia latifolia*, *Glycyrrhiza glabra*, *Malva rotundifolia*, *Onosma bracteatum*, *Viola odorata* and *Zizyphus jujuba*. Five different species of bacteria were subjected for antibacterial activity of the components of Joshanda by Abdul *et al*. The antimicrobial activity of individual components of Joshanda was determined by agar well diffusion method. Their results indicated that *Zizyphus jujuba*, *Onosma bracteatum* and *Glycyrrhiza glabra* have significant degree of *in-vitro* activity against *S. aureus* while *Cordia latifolia* has got a significant *in-vitro* activity against *H. influenza* responsible for common cold. Other ingredients did not show any significant activity against rest of the organisms tested. [16]

CORSHE-E is a polyherbal combination which contains extracts of *Adhatoda vasica*, *Glycyrrhiza glabra*, *Terminalia belerica*, *Solanum xanthocarpum* and *Ocimum sanctum*. Clinical validation of the efficacy and safety of herbal cough formula CORSHE-E of ayurvedic origin was carried out by Tanuja *et al*. An open label, uncontrolled clinical study was done on thirty patients with history of cough. The patients were given the cough syrup after they were enrolled in the study and were followed up for a period of seven days. The cough severity, frequency (as recorded on Visual Analogue Scale from 0 to 10 cm), chest discomfort, quantity and type of sputum were recorded at screening, on the fourth day and on the seventh day of treatment. The patient recorded the severity and frequency of cough on a Visual Analogue Scale which was divided into ten equal parts of 1 cm each. The patient marked the extent of symptoms on this scale at screening and after four days of consumption of the cough syrup. The scores were marked on these days and reduction in score was examined for efficacy evaluation of the cough syrup. The clinical and hematological safety parameters and parameters for acceptability of cough syrup (palatability, color, odor and consistency) were also studied. Global assessment by the patient and the physician was also carried out on the fourth day. The test drug CORSHE-E was found to be effective and safe cough syrup which was highly acceptable for patients with cough of short duration. [17]

Evaluation of antitussive activity of Honikof syrup which is a combination of herbal medicines as formulations in sulphur dioxide induced cough model in rats was studied by Lucia *et al*. Honikof syrups contains *Ocimum sanctum*, *Glycyrrhiza glabra*, *Adhatoda vasica*, *Zingiber officinale*, *Piper longum*, *Curcuma longa*, *Piper nigrum*, *Pudina satva*. Honikof tablets contain these same herbs with different quantities and Herbigor Honey and Lemon Syrup. The herbal formulations demonstrated significant (P<0.05) antitussive activity in sulphur dioxide induced cough model. Thus their study showed that the polyherbal formulation have significant (P<0.05) antitussive effect in experimentally induced cough reflex in rats comparable to the

standard drug codeine phosphate and this provides pharmacological evidence in support of these herbal products as antitussive agents. [18]

A randomised, double-blinded, placebo-control study comparing of a polyherbal preparation with a placebo was conducted in 82 patients, who attended the Family Medicine Training Centre, Prince of Wales Hospital, Hong Kong between November and December, 2003 by Wong *et al*. The herbal preparation includes nine commonly used Traditional Chinese Medicinal (TCM) herbs for cough such as *Bulbus fritillariae cirrhosae*, *Herba schizonepetae*, *Radix ledebouriellar*, *Radix platycodi*, *Radix glycyrrhizae*, *Radix asteris*, *Radix stemonae*, *Rhizoma cynanchi stannotonii* and *Pericarpium citri reticulatae*. The treatment was done for 5 days and the patients were followed-up for another 6 days. Patients were asked to fill in a cough score and validated Leicester cough questionnaire (LCQ). TCM was well-tolerated and received among the Hong Kong Chinese population. This TCM preparation appeared to have some beneficial effects in the treatment of cough. [19]

Polyherbal formulation used in treatment of upper respiratory tract infection: A double-blind controlled trial was aimed to investigate the clinical effects of aromatic essential oils in patients with upper respiratory tract infections by Eran *et al*. The trial was conducted in six primary care clinics in northern Israel. A spray containing aromatic essential oils of five plants (*Eucalyptus citriodora*, *Eucalyptus globulus*, *Mentha piperita*, *Origanum syriacum* and *Rosmarinus officinalis*) as applied 5 times a day for 3 days and compared with a placebo spray. The main outcome measure was patient assessment of the change in severity of sore throat, hoarseness or cough. Sixty patients participated in the study (26 in the study group and 34 in the control group). The results showed that those 20 minutes following the spray use, participants in the study group reported a greater improvement in symptom severity compared to participants in the placebo group. There was no difference in symptom severity between the two groups after 3 days of treatment. Therefore the spray application of five aromatic plants reported in their study brings about significant and immediate improvement in symptoms of upper respiratory ailment. This effect is not significant after 3 days of treatment. [20]

Actovet CRD (A.CRD) is a polyer formulation consisting of *Glycorrhyza glabra*, *Adhatoda vasika*, *Pipper longum*, *Abis Webbiana*, *Azadirachta indica* and *Curcuma longa*, which have known therapeutic effect on respiratory system and other systemic diseases with positive effect to boost immunity. To find out the efficacy of A.CRD and to optimize its level of supplementation against the chronic respiratory disease (CRD) three age groups of broilers viz., 0 day, 14 day and 28 day representing the age groups of 0-2 weeks (T1), 2-4 weeks (T2) and >4 weeks (T3) of age respectively were isolated for the experiment from a large size group of birds from each of five farmers by Rudraswamy *et al*. The results of the trial indicated that A.CRD improved the body weight gain, survivability, haemoglobin, PCV, total protein levels significantly ($P \leq 0.05$). The symptoms of the CRD in the infected birds subsided within a week period of treatment. The birds stopped gasping, rales and other symptoms of the CRD within 4-7 days of treatment at all therapeutic dosage levels. The results indicated that the birds of age group T1, T2 and T3 should be supplemented with A. CRD at the rate of 10, 20 and 40 ml/100 birds respectively. The birds did not show any symptoms of drowsiness, off feed which is usually observed in antibiotic treatment. The results showed that A. CRD can replace antibiotic therapy. Hence, this herbal formulation can be used for prevention and treatment of chronic respiratory disease and a suitable supplement for organic poultry farming. [21]

A polyherbal formulation named as SIVA syrup was made with different herbs such as *Indigofera aspalathoides*, *Celastrus paniculates*, *Corallocarpus epigaeus*, *Solanum trilobatum*, *Wrightia tinctoria*, *Bacoba monnieri*, *Piper longum*, *Piper nigrum*, *Zingiber officinale*, *Tinospora cordifolia*, *Leucas aspera* and *Piper betle*. Respiratory syncytial virus (RSV) is the chief cause of most of the upper respiratory infections in human being. Evaluation of the immunomodulatory effect of polyherbal formulation (SIVA syrup) against RSV infection in animal model was done by Krishnamoorthy *et al*. Results of the studies suggested that polyherbal formulation of medicinal plants is a very potent immunomodulator and has a significant role in the treatment of upper respiratory infections in human being. [22]

Polyherbal formulation used in Chronic Obstructive Pulmonary Disease: Bresol®- a polyherbal formulation contains *Curcuma longa*, *Cinnamomum zeylanicum*, *Elettaria cardamomum*, *Cinnamomum tamala*, *Embelia ribes*, *Cyperus rotundus*, *Mesua ferrea*, *Ocimum sanctum*, *Adhatoda vasica*, Trikatu and Triphala, was evaluated in an experimental model of cigarette smoke (CS)-induced Chronic Obstructive Pulmonary Disease (COPD) in rats. Ten minutes daily exposure to CS for 7 weeks caused significant elevation of TNF-α ($P<0.01$) and total protein ($P<0.01$) in the bronchoalveolar lavage fluid (BALF) of positive untreated control animals, indicating ongoing inflammatory process in the lungs. Further, histopathological findings have confirmed the presence of pathological lesions in the trachea and lungs. Five weeks of post-treatment with Bresol® (250 and 500 mg/kg, *p.o*.) showed significant and dose-dependent anti-inflammatory effects against CS-induced lung abnormalities by maintaining the TNF-α and total protein levels within the normal range. Additionally, Bresol®-treated animals showed normal cyto-architecture of the trachea and lungs. Thus Bresol® showed dose-dependent protection against CS-induced lung and tracheal injury in rats, which further indicate,

Bresol® is a useful healing agent, may help to decelerate the progression of COPD and reduce the exacerbations in patients. [23]

The evaluation of the anti-inflammatory effect of PM014, a poly herbal formulation contains 7 species of medicinal plants on cigarette smoke induced lung disease in the murine animal model of chronic obstructive pulmonary disease (COPD) was done by Kyung-Hwa *et al*. Mice were exposed to cigarette smoke (CS) for 2 weeks to induce COPD-like lung inflammation. Two hours prior to cigarette smoke exposure, the treatment group was administered PM014 via an oral injection. The efficacy of PM014 was compared with that of the recently developed anti-COPD drug, roflumilast. Results obtained from their study showed that PM014 substantially inhibited immune cell infiltration (neutrophils, macrophages and lymphocytes) into the airway. In addition, IL-6, TNF-α and MCP-1 were decreased in the BAL fluid of PM014-treated mice compared to cigarette smoke stimulated mice. These changes were more prominent than roflumilast treated mice. The expression of PAS-positive cells in the bronchial layer was also significantly reduced in both PM014 and roflumilast treated mice. These data suggested that PM014 exerts strong therapeutic effects against CS induced, COPD-like lung inflammation. [24]

PM014 is a polyherbal formulation contains root of *Stemona sessilifolia*, root of *Asparagus cochinchinensis*, root of *Scutellaria baicalensis*, fruit of *Schizandra chinensis*, Root of *Rehmannia glutinosa*, seed of *Prunus armeniaca* and Cortex of *Paeonia suffruticosa*. Chronic obstructive pulmonary disease (COPD), which is characterized by airway obstruction, leads to, as the two major forms of COPD, chronic bronchitis and emphysema. A study was conducted to evaluate the effects of herbal formula, PM014, in a murine model of COPD. Balb/c mice were treated once with each herb extract in PM014 or PM014 mixture via an oral injection. Lipopolysaccharide (LPS) or elastase/LPS were administrated to the mice to induce a disease that resembles COPD. PM014 treatment significantly attenuated the increased accumulation of immune cells in bronchoalveolar lavage fluid (BALF) compared to control mice. In addition, the TNF-α and IL-6 levels in BALF were decreased in the PM014 mice. Furthermore, histological analysis demonstrated that PM014 attenuated the hazardous effects of lung inflammation. These data suggest that PM014 exerts beneficial effects against forms of COPD such as lung inflammation. This study provides evidence that treatment with PM014 exerts preventive and therapeutic effects against COPD-like animal models in mice. The remarkable effect exerted by PM014 suggests that it has the potential for use in the treatment of lung inflammation. [25]

Polyherbal formula used in the treatment of severe acute respiratory syndrome

The polyherbal formulation consists of 12 herbs, namely *Folium mori*, *Flos chrysanthemi*, *Semen armeniacae*, *Fructus forsythiae*, *Herba menthae*, *Radix platycodonis*, *Radix glycyrrhizae*, *Rhizoma phragmitis*, *Radix astragali*, *Radix saposhnikoviae*, *Folium isatidis* and *Radix scutellariae*. An investigation the efficacy of this herbal formula in the prevention of severe acute respiratory syndrome (SARS) transmission among health care workers and also to evaluate the safety of this formula was done by Joseph *et al*, during epidemic of SARS at Hong Kong. Two cohorts of health care workers from 11 hospitals in Hong Kong, 1 using an herbal supplement for 2-week period (n = 1063) and a control cohort comprising all other health care workers who did not receive the supplement (n = 36, 111) were compared prospectively taking this herbal supplement for 2-week period. SARS attack rates and changes in quality of life and influenza-like symptoms were also examined at three time points among herbal supplement users. None of the health care workers who used the supplement subsequently contracted SARS compared to 0.4% of the health care workers who did not use the supplement. Improvements in influenza like symptoms and quality of life measurements were also observed among herbal supplement users. Less than 2% reported minor adverse events. The results of this pilot study suggested that there is a good potential of using Traditional Chinese Medicine (TCM) supplements to prevent the spread of SARS. [26]

Polyherbal formulation used in treatment of rhinitis:

A combined herbal therapy (ARND) against perennial allergic rhinitis was tested in a randomized, double-blinded and placebo-controlled setting, with a crossover arrangement for the administration of allergic rhinitis nasal drop or placebo by Chui et al. ARND consisted of *Herba centipedae* 23%, *Herba menthae* 16%, *Radix paeoniae alba* 16%, *Radix scutellariae* 10%, *Radix glycyrrhizae* 6%, *Radix platcodi* 6%, *Flos lonicerae* 5%, *Fructus zizyphi jujubae* 5%, *Rhizoma coptidis* 4%, *Radix ledebouriellae* 5% and *Pericarpium citri reticulatae* 4%. Each of these herbal remedies has anti-bacterial and anti-inflammatory activities. ARND relieved clinical symptoms in patients with perennial allergic rhinitis and improved their quality of life. [27]

Bresol (HK-07) tablet is a polyherbal formulation contains extracts of *Curcuma longa*, *Ocimum sanctum*, *Adhatoda vasica*, Trikatu, Triphala, *Embelia ribes*, *Cyperus rotundus*, *Cinnamomum zeylanicum*, *Elettaria cardamomum*, *Cinnamomum tamala* and *Mesua ferrea*. A non-comparative phase III clinical trial was conducted by Kalpana and Kolhapure in the year of 2004, at Bai Jerbai Wadia Hospital for Children, to evaluate the efficacy and safety of Bresol (HK-07) tablets in upper and lower respiratory tract allergic diseases by taking one hundred and five children from the age group of 3 to 12 years who presented with symptoms of rhinitis or bronchitis. All children were investigated by hematological and biochemical tests and PEFR recording was done to determine the functional lung capacity. All children were followed up fortnightly for

a period of three months. All children were investigated by hematological and biochemical tests along with PEFR at the end of the study period. All adverse events were recorded with information about severity, onset, duration and action taken regarding the study drug. There was a highly significant reduction in mean scores for sneezing, nasal congestion, itching of the eyes and nose, postnasal drip, rhinorrhea, watery eyes and total rhinitis symptom score at the end of the study. There was also a significant reduction in mean scores of chest tightness, daily asthmatic symptoms, wheezing, shortness of breath, cough, sputum production and total asthma symptom score at the end of study. Their study concluded that, Bresol (HK-07) tablets are clinically effective and safe in children suffering from allergic rhinitis or allergic bronchitis or asthmatic bronchitis without any clinically significant adverse events. [28]

Clearguard a polyherbal tablet consisting of *Cinnamomum zeylanicum*, *Malphighia glabra* and *Bidens pilosa* was screened against allergic rhinitis in a randomized, double-blinded crossover trial by Corren *et al*. The results of clearguard were compared with the positive control treatment with loratadine and placebo. The polyherbal tablet significantly reduced nasal symptoms and inhibited the release of prostaglandin D2 in nasal lavage analysis. [29]

Shi-Bi-Lin (SBL) a polyherbal remedy consisting of *Xanthium sibiricum*, *Angelica dahurica*, *Radix apiaceae*, *Saposhnikovia divaricata*, *Magnolia biondii*, *Gentiana scabra* and *Verbena officinalis*. A study was conducted to evaluate the effect of SBL on allergic rhinitis both *in-vivo* and *in-vitro* by Zhao *et al*. The results of their study showed that SBL can suppress eosinophil infiltration in animal's nasal tissues and inhibited the expression of endothelial nitric oxide synthase and release of thromboxane B2, which are playing an important role in the acute phase of inflammation. [30]

Polyherbal formulation used in treatment of bronchitis: The efficacy of a polyherbal Unani formulation contains *Pistacia integerrima*, *Glycyrrhiza glabra*, *Piper nigrum* and Salt of barley was evaluated in chronic bronchitis by Tariq *et al*. During their study 40 patients were randomly selected into two groups. The first group (n = 20) was of test study and other group (n = 20) for placebo study. Both, placebo and test groups were received 3 grams of sample in powder form twice daily for four weeks by oral route. Severity of cough, sputum, breathlessness, wheezing, peak expiratory flow rate (PEFR) and chest X-ray at the beginning and the end of treatment were taken into account. The test drug showed a significant improvement as compared to placebo. This study showed that the polyherbal Unani formulation has the significant role in chronic bronchitis which is well recognized in Unani classical literature also. [31]

Polyherbal formulation used in treatment of tonsillitis: A Japanese polyherbal combination containing *Radix bupleuri*, *Tuber pinelliae*, *Radix scutellariae*, *Radix platycodi*, *Fructus jujube*, *Radix panacis*, *Radix glycyrrhizae* and *Rhizoma zingiberis* was prepared and shown to be effective in chronic and recurrent tonsillitis. After one year of treatment, the incidence of acute tonsillitis in patients with chronic tonsillitis decreased in seven of ten cases. [32]

Koflet, a polyherbal formulation contains herbs such as *Acacia catechu*, *Syzygium aromaticum*, *Terminalia chebula*, *Elettaria cardamomum*, *Cinnamomum zeylanicum*, *Glycyrrhiza glabra*, *Curcuma longa* and *Vitis vinifera*. The efficacy of Koflet lozenges was studied in patients with acute or chronic tonsillitis or pharyngitis by Prakash *et al*. Forty eight patients of either sex aged 18-60 years were taken for the study to test the efficacy and tolerability of Koflet lozenges. Twenty three of them had catarrhal pharyngitis, sixteen had catarrhal tonsillitis and nine of them had both. The dosage was 3 lozenges every 8 hours for 3 days in patients with sore throat and related signs and symptoms. The patients were evaluated every day for three days. At the end of the 3 day treatment, they were evaluated for the efficacy and tolerability of Koflet lozenges. Results of the study showed that Koflet was found to be effective moderately in 16.66%, good in 70.83% and excellent in 10.41%, while in one patient (2.08%) there was no response. There was no untoward incident in any of the patients. Koflet lozenges were well tolerated and no patients reported any adverse event. [33]

A double-blind, placebo-controlled clinical trial was conducted by using a polyherbal capsule. The study was carried out with Lung Support Formula or identical placebo capsules. The Lung Support Formula capsules were manufactured following current Good Manufacturing Practices (cGMP) guidelines by Robinson Pharma, Inc. (Orange County, CA, USA). The main ingredients of the Lung Support Formula capsules included *Astragalus membranaceus*, *Cordyceps sinensis*, *Ophiopogon japonicus*, *Panax ginseng*, *Morus alba*, *Ginkgo biloba*, *Prunus armeniaca*, *Forsythia suspensa*, *Salvia miltiorrhiza*, *Gekko gecko*, vitamin A, vitamin C, magnesium and zinc. The placebo was also manufactured by Robinson Pharma with the main ingredients being Calcium, Maltodextrin and Rice Flour. This clinical research support to the hypothesis that the proprietary formula, Lung Support Formula, which contains naturally derived Chinese herbal medicines and it is useful in significant improvement of respiratory symptoms and is well-tolerated in short-term use among older adults. [34]

Polyherbal formulation used in treatment of diabetes: APKJ-004, the polyherbal extract prepared from the seeds of *Eugenia jambolana* and barks of *Cinnamomum zeylenicum* as hydro alcohol and aqueous extracts. A study was designed by Padmanabha *et al*, for assessment of toxicity and therapeutic efficacy (antidiabetic activity) of the polyherbal extract APKJ-004. The acute and sub acute toxicity were conducted in wistar rats. The results of toxicity assessment revealed

that clinical, biochemical and histopathological parameters studied were in normal range and comparable to controls. The study revealed that no toxic symptoms observed throughout the period of exposure. Based on the results obtained it was concluded that APKJ-004 polyherbal extract act as a potent antidiabetic agent with minimal or no side effects and useful in the pharmacotherapy of diabetes. [35]

Madhumeh, a polyherbal preparation was investigated to validate the antidiabetic claim in streptozotocin-nicotinamide induced diabetic rat model by Vinod *et al*. Evaluation of antidiabetic activity of polyherbal formulation in Streptozotocin-Nicotinamide induced diabetic in rats and induction of diabetes in animal and estimation of biochemical parameters were taken into account. Madhumeh possesses blood glucose lowering properties comparable to standard oral hypoglycemic agent glibenclamide. Madhumeh showed marked increase in total protein in diabetic treated and lower the level of triglyceride in serum. Body weight, food intake, water intake are improved in formulation treated rats compared to diabetic rats suggesting the returning of glucose uptake utilization back to normal levels. [36]

A polyherbal formulation (OB-6) was prepared by David *et al*, using extracts of six medicinal plants such as *Cassia angustifolia*, *Nigella sativa*, *Phyllanthus amarus*, *Emblica officinalis*, *Zingiber officinale* and *Terminalia chebula*. A study was undertaken to evaluate Anti-hyperlipidemic potentials through *in-vivo* methods of OB-6 prepared in-house. The rats were fed with high fat diet for the induction of hyperlipidemia for two weeks. Upon confirmation of disease induction the animal experiments were conducted as per standard protocols. The hyperlipidemic rats were administered three graded doses of OB-6 and the standard control group was treated with Atorvastatin (30 mg/kg) orally for 14 days. After treatment for ten days, blood samples from the OB-6/standard/vehicle were collected and lipid profile, atherogenic index and atherogenic ratio were determined. After sacrificing the animal, histopathological study suggested that OB-6 produced significant hypocholesterolemic effect. [37]

A study was conducted to evaluate hypoglycemic and weight stabilizing effects of a compound herbal formulation named Ziabeen in normal and alloxan induced diabetic in rabbits by Muhammad et al. Diabetes was induced by alloxan mono hydrate. Blood glucose levels of animals were determined after oral administration of 2, 3 and 4 g/kg body weight of powdered Ziabeen tablets, unit doses of insulin, also a combination of insulin and Ziabeen, and 1 mg/kg body weight of pioglitazone (positive control) as a single dose/day both in normal and alloxan-diabetic rabbits. Blood glucose levels were measured at 0, 2, 4, 6 and 8 h intervals after administering the drugs. Highly significant (P<0.001) reduction in blood glucose was observed at all time intervals with 4 g/kg of Ziabeen. A synergistic hypoglycemic effect of oral Ziabeen with insulin injection was also observed. Oral glucose tolerance test results showed that 4 g/kg of Ziabeen significantly reduced blood glucose levels for 5 h. When Ziabeen and pioglitazone were given as repeated doses for 30 days, substantial reduction in blood glucose levels was observed in alloxan-diabetic rabbits. [38]

Anti-hyperlipidemic property of Triglize, a polyherbal formulation was determined in male albino Wistar rats by Parasuraman *et al*. The aqueous extract of polyherbal formulation (PHF) triglize was used for the study. The animals were fed with high fat diet to induce hyperlipidemia. The test (polyherbal formulation) and standard drugs were administered once dally as a single oral dose for 28 days. The test drug administered at the dose levels of 25, 50, 100 and 200 mg/kg and standard drug atorvastatin was administered at the dose level of 10 mg/kg. Weekly body weight variation, lipid profile (total cholesterol, triglyceride, HDL, VLDL and LDL levels, HDL ratio and atherogenic index) were analyzed and day of the termination the liver was isolated from all the animals and subjected to histopathological evaluation. The PHF has been found significant anti-hyperlipidemic and hepatoprotective action. Their study concluded that, the "Triglize" a polyherbal formulation has anti-hyperlipidemic property against high fat diet induced hyperlipedemia in rats. [39]

LI85008F or Adipromin is a polyherbal formulation comprised of ethanol extract of *Moringa olefera* leaves, aqueous alcohol extract of *Murrya koenigii* leaves and ethanol extract of *Curcuma longa* rhizomes were mixed at a ratio of 6: 3: 1, respectively. LI85008F was evaluated its efficacy on weight loss in obese human subjects in an 8-weeks randomized, double-blind, placebo-controlled study by Krishanu *et al*. Fifty obese subjects were randomized into two groups; placebo (n = 25) and LI85008F formulation (n = 25). The participants received either 900 mg/day of LI85008F formulation in three divided doses or three identical placebo capsules and all of them remained on a calorie-controlled diet (2000 cal/day) and 30 min walking for 5 days a week during the entire duration of the study. At the end of the trial period, LI85008F supplemented group showed significant net reductions in body weight and Body Mass Index (BMI). The participants, who received the herbal formulation, showed reduced fasting blood glucose, LDL, LDL/HDL ratio and triglycerides. No major adverse events were reported by the participants in their study duration. The herbal formulation LI85008F (Adipromin) is prepared from commonly used medicinal plants extracts, which provides useful and safe application for weight loss in obese humans. It also demonstrates potential promise in controlling healthy blood glucose level in obesity linked type 2 diabetes. [40]

Diabecon (D-400), a herbomineral anti-diabetic preparation, was studied for its pharmacokinetic interaction with the commonly used drugs rifampicin and nifedipine by Mitra *et al*. The pharmacokinetic interaction of rifampicin and Diabecon (D-400) was studied in animal models by using rabbits as well as in healthy human volunteers. The results of their studies revealed that Diabecon (D-400) did not alter the pharmacokinetic profiles of rifampicin and nifedipine. [41]

SAAAB as a polyherbal formulation used for the treatment of Ataxia. Ataxia is a complication of high blood pressure and diabetes with a clear cut deficiency of ubiquinone central to depletion of vitamins notably vitamin E. A study was conducted to determine the presence of ubiquinone contained in SAAAB as it was evidence in a remarkable improvement in area of cerebral dysfunction improvement and a notable decrease in the ICARS' score after six months of supplementation by Amodu *et al*. SAAAB with Vernoniaamygdalina as it active ingredient had been used in traditional medicine for the treatment of various ailments, it has been used to treat gastrointestinal disorders, haematoma, malaria, inflammation, cancer, ataxia etc. sequel to this finding, it has become clear that ataxia can be effectively managed with the concoctions infused from cocktails of fruits and vegetables with the abundance of ubiquinone contained in the supplement-SAAAB. [42]

A polyherbal formulation was prepared by using *Tribulus terrestris*, *Piper nigrum*, *Ricinus communis* by Baldi *et al*. A study was designed to evaluate the effect of a four weeks treatment of this polyherbal formulation at doses of 100, 200 and 300 mg/kg on blood glucose level and other biochemical parameters like cholesterol, urea, creatinine, billirubin and SGPT in alloxan (150 mg/kg, IP) induced diabetic rats. Oral administration of polyherbal formulation to diabetic animals up to four weeks dose dependently reduced the blood glucose level, which was comparable to that of glibenclamide (5 mg/kg). Significant decrease in body weight also observed with diabetic control, which was partially restored upon administration of polyherbal formulation. The polyherbal formulation also reduced elevated levels of selected biochemical parameters and prevented other complication of hyperglycemia. These findings provide scientific evidences to anti-diabetic use of a traditional formulation and suggest that administration of polyherbal formulation to rats, in a dosage used safely by humans, reduces the production of various diabetes causing biochemical parameters and concomitantly prevents the development of Type-2 (NIDDM) diabetes in established animal models. [43]

NIDDWIN a polyherbal formulation which includes 11 antidiabetic herbs such as *Tinospora cordifolia*, *Gymnema sylvestre*, *Terminalia tomentosa*, *Tribulus terrestris*, *Emblica officinalis*, *Mucuna pruriens*, *Sida cordifolia*, *Withania somnifera*, *Terminalia belerica*, *Terminalia chebula* and *Momordica charantia*. A study was focused by Sruthi *et al*, to evaluate the antidiabetic activity and antioxidant activity of NIDDWIN in alloxan induced diabetic rats. NIDDWIN showed significant antidiabetic activity at 4th hr on 1st, 5th and 10th day was found to be effect in comparable with standard Glibenclamide 10 mg/kg. Histopathological results of NIDDWIN showed positive results when compared with standard Glibenclamide 10 mg/kg. NIDDWIN significantly showed the percentage reduction of lipid per-oxidation levels in diabetic rats. Their study suggested that the polyherbal formulation NIDDWIN possess a potent antidiabetic activity as it significantly reduced blood glucose levels and also showed antioxidant activity in diabetic rats. In addition to this it has also shown to reduce cholesterol, triglyceride levels in diabetic rats. [44]

Baker Cleanser Bitters (BCB) - a polyherbal formula commonly used in the treatment of diabetes, liver cirrhosis, kidney failure, rheumatism and arthritis was evaluated in an acute and sub-chronic toxicity study in Wistar albino rats by Patrick-Iwuanyanwu *et al*. A single administration of BCB was given orally at the highest dose level of 2000 mg/kg body weight in the acute toxicity study. There were no mortalities or clinical signs observed in rats in the acute toxicity study. In the sub-chronic study in rats, daily oral administration of BCB at the dose of 200 mg/kg body weight resulted in a drop in percentage increase in body weight at the end of the 4th week. The study also revealed that the polyherbal drug may have good hypoglycemic effects and favourable reducing effects on the cardiovascular risk factors and explains the basis for the continual use of this plant by traditional medical practitioners. [45]

Polyherbal formulation having immunomodulatory effects: Triphala is a polyherbal formulation, comprising of the fruits of *Emblica officinalis*, *Terminalia belerica* and *Terminalia chebula*. An attempt has been made by Evan Prince *et al*, to evaluate the immunomodulatory effects of the Indian ayurvedic herbal formulation Triphala on experimental induced inflammation. The effect of Triphala was investigated on complement activity, humoral immune response and cell mediated immune response in mice and in mitogen (phytoheamagglutinin)-induced T-lymphocyte proliferation *in-vitro*. Triphala administration significantly inhibited the complement activity, humoral and cell mediated immune response (delayed type hypersensitivity reaction (DTH)) and mitogen (phytohaemagglutinin)-induced T-lymphocyte proliferation in a dose dependent manner. These observations suggested that Triphala caused immunosuppression in experimental induced inflammation, indicating that they may provide an alternative approach to the treatment of inflammatory and autoimmune diseases. [46]

Polyherbal formulation having anti-inflammatory activity: Sudard is a poly-herbal formulation containing extracts of 11 medicinal plants. Each tablet contains *Commiphora mukul*, *Pluchea lanceolata*, *Paederia foetida*, *Vitex negundo*, *Zingiber officinalis*, *Ricinus communis*, *Lepidium sativum*, *Colchicum luteum*, *Smilax glabra*, *Strychnous nuxvomica* and *Shilajatu pitch*. A study was aimed by Mohammed *et al*, to evaluate the efficacy of sudard using different animal models such as formalin (2% v/v)-induced acute inflammation, carrageen (1% v/v)-induced polyarthritis, adjuvant-induced arthritis, effect on sub acute inflammation by sponge implantation technique and analgesic activity by Eddy's hot plate method. Their results indicate that the formulation sudard possesses good anti-inflammatory, anti-arthritic and analgesic activities in the experimental animal models. [47]

The Brazilian polyherbal formulation (BPF) is composed of *Eucalyptus globulus*, *Peltodon radicans* and *Schinus terebinthifolius* in alcohol. The formulation is popularly used in Paraia state, Brazil since 1889 and it is used as an antiseptic and anti-infl ammatory medicine. A study was aimed by Karina *et al*, to evaluate the anti-inflammatory property of the polyherbal formulation. For this purpose it was used the 12-O-tetradecanoylphorbol 13-acetate (TPA) and capsaicin-induced mouse ear edema and the carrageenan-induced rat paw edema. The BPF at dose of 26 mL/Kg inhibited both 12-O-tetradecanoylphorbol 13-acetate (TPA) and capsaicin-induced ear edema by 49% (P<0.05) and 24% (P<0.01) respectively. Preliminary results on carrageenan-induced rat paw edema demonstrated that oral administration also inhibited the paw edema by approximately 29%. The results demonstrated that the Brazilian polyherbal formulation has anti-inflammatory activity. [48]

Polyherbal formulation having antipyretic activity: JURU-01 is a polyherbal formulation that contains *Adhathoda vasica*, *Andrographis paniculata* and *Moringa oliefera*. The antipyretic activity of JU-RU-01 was evaluated in Brewers Yeast induced pyrexia in Wistar rats by Rabish *et al*. The formulation (150 and 300 mg/kg) showed very significant reduction of yeast induced pyrexia in rats with respect to control group. The antipyretic activity of the extract was comparable to the standard prototype, paracetamol. The antipyretic activity of the polyherbal formulation increases significantly at the dose of 300 mg/kg having P<0.01 at first, second and fourth hour. [49]

Polyherbal formulation having anti-microbial activity: Ade & Ade Antidiabetic®, an antidiabetic polyherbal formulation, prepared with *Ocimum gratissimum*, *Citrullus lanatus*, *Momordica charantia*, *Chrysophyllum delevoyi* and *Uncaria tomentosa* leaves. Microbial purity was evaluated on some bacterial and fungal organisms using appropriate diagnostic media. Acute toxicity of the polyherbal formulation was evaluated in Swiss albino mice by administering orally graded doses of the lyophilized formulation in the ranges of 1.0 g to 20.0 g/kg body weight to the animals and observed continuously for the first 4 hours and hourly for the next 12 hours then 6 hourly for 56 hours (72 h). Wistar rats were also fed with different doses of the lyophilized formulation for 30 days and the effects on the body weight, biochemical and hematological profiles and tissue histology were evaluated (sub acute toxicity model). The presence of *E. coli* bacterial organisms with loads above officially accepted limit were observed in the formulation. The median acute toxicity value (LD_{50}) of the polyherbal formulation was determined to be 15.0 g/kg body weight. The extract significantly increased (P<0.05) hemoglobin and RBC contents in all the treated groups compared to the control. There was also an increase in WBC which was complemented by an increase in lymphocyte cells. The formulation however exhibited hypolipidaemic and hypoglycemic activities and good reducing effects on cardiovascular factors. The tissue histology also revealed that the formulation did not provoke toxic effect on the animals organs at the doses administered. [50]

A polyherbal hand wash was prepared by using extracts of *Sida cardifolia*, *Azadirachta indica*, *Aloe vera* gel and lemon juice by Jyothi *et al*. The anti-microbial activity of the prepared polyherbal hand wash was tested against the skin pathogens like *Putida vulgaris*, *Staphylococcus aureus*, *Bacillus subtilis* and its efficiency was verified using dip-well method and the results obtained were compared with the commercially available hand wash. The results from dip well method shown that the hand wash prepared from methanol extract of the combined plant material have greater activity than the commercially available hand wash. The better activity of the prepared formulation may be due to the combined activity of phytoconstituents present in the extracts. Thus, these compounds can be extracted and incorporated in bases in order to prepare superior antimicrobial hand wash with less or no side effects. [51]

Polyherbal syrup (66.67% w/v) was prepared as per Indian pharmacopoeia. 200 mg of each extracts of *Terminalia chebula*, *Mentha piperita*, *A. vasica*, *Zingiber officinale* and 400 mg of each extracts of *O. sanctum*, *Glyzyrrhiza glabra*, *Withenia somnifera* and *Piper longum* were used to prepare the polyherbal syrup. The prepared syrup was investigated for their antitussive effect on citric acid induced cough model in guinea pig by Meher *et al*. The results showed that the formulated cough syrup exhibited significant antitussive activity in a dose dependent manner and the activity was compared with the prototype antitussive agent diphenhydramine HCl. It is found that antitussive activity produced by the herbal formulation in the minimum dose was much better than the standard drug. It can be concluded that the formulated polyherbal cough syrup in 1 ml exerts a significant antitussive effect in experimentally induced cough

reflex in mice comparable to the standard drug Diphenhydramine hydrochloride. [52]

A polyherbal preparation was prepared from the decoction of the aerial parts of *Rhynchosia recinosa*, the stem barks of *Ozoroa insignis*, *Maytenus senegalensis*, *Entada abyssinica* and *Lannea schimperi* and evaluated for its safety and efficacy. The individual extracts and polyherbal preparation were tested for antibacterial activity against four Gram negative bacteria; *Escherichia coli* (ATCC 25922), *Salmonella typhi* (NCTC 8385), *Vibrio cholerae* (clinical isolate) and *Klebsiella pneumoniae* (clinical isolate) using the microdilution method by Emmanuel *et al*. In addition the extracts were evaluated for brine shrimp toxicity and acute toxicity in mice. The combined extract of the five plants exhibited a dose-dependent protective activity in the rat ethanol-HCl gastric ulcer model. The extracts also exhibited weak antibacterial activity against four Gram negative bacteria and low acute toxicity in mice and brine shrimps. [53]

A polyherbal unani formulation 'Laooq Sapistan Khyaar Shambari' (LSKS) was used to screen for its probable antibacterial activity by Abdul *et al*. Laooq Sapistan Khyaar Shambari (LSKS) is a polyherbal Unani formulation used in Unani System of Medicine for the treatment of various upper respiratory tract ailments. This formulation was selected to evaluate its probable antibacterial activity by disk diffusion and Broth dilution method against gram positive bacterial strains (*Staphylococcus aureus*, *Bacillus cereus*, *Corynebacterium xerosis*, *Streptococcus mutans* and *Staphylococcus epidermidis*) and gram negative bacterial strains (*Klebseilla pneumoniae* and *Pseudomonas aeruginosa*). Results revealed that the formulation exhibits significant antibacterial activity against gram +ve and gram -ve bacterial strains. It was concluded that the claims of Unani physician for the usefulness of LSKS in upper respiratory tract infections are in consonance as described by them. The potent antibacterial activity so found could be due to various bioactive constituents present in the various ingredients of this Unani compound formulation which interact in complex ways to produce the needed therapeutic effect as a whole. It can be concluded that LSKS has an effective antimicrobial property probably due to the presence of various pharmacologically active components. [54]

An antiseptic polyherbal ointment was formulated using methanolic extract of *Azadirachta indica*, *Chromolaena odorata*, *Mimosa pudica*, *Samadera indica* and evaluated for its physicochemical property, antibacterial and antioxidant activity by Rajasree *et al*. Ointments were prepared using different concentrations of the extracts such as 2%, 4%, 6% w/w by fusion method using emulsifying ointment as base. Formulations were then tested for its physicochemical properties like loss of drying, pH, spreadability, extrudability and diffusion study and gave satisfactory results. The prepared formulations were also stable at 4ºC, 25ºC and 37ºC. Further, polyherbal formulations were evaluated for its anti-bacterial activity against *Staphylococcus aureus*, Pseudomonas sp., Bacillus sp., by agar diffusion method by using Betadine (5%w/w) as the standard. All the formulations showed predominant activity against selected species. Formulations were also evaluated for antioxidant activity through reducing power assay, nitric oxide and hydrogen peroxide scavenging method. The results showed that the scavenging activity of the formulations increased with increase in concentration and this is due to the presence of flavonoids and tannins. The presence of both antibacterial and antioxidant activity reveals that the prepared ointment can also be used for wound healing and is an effective polyherbal antiseptic ointment. [55]

Polyherbal formulation having antioxidant activity:

Avaleha a polyherbal semisolid formulation containing *Hippophae rhamnoides*, *Emblica officinalis*, *Allium prezewalskianum*, *Bidense pilosa*, *Centaurea depressa*, *Inula racemosa*, *Rubia cordifolia*, *Capparis spinosa*, *Ephedra gerardiana*, *Foeniculum vulgare*, *Mentha spicata*, *Arnebia euchroma*, *Bunium persicum*, *Ocimum sanctum*, *Clarified butter*, *Sisamum indicum* and *Saccharum officinalis* was prepared based on the methodology described in Ayurvedic formulary of India for Avaleha preparation and tested for antioxidant activity. *In vitro* antioxidant study was done by DPPH free radical scavenging activity assay using ascorbic acid as standard by Bhawana *et al*. The results obtained in their study indicated that the formulation showed significant antioxidant activity. This signifies that combination of herbs can make a good antioxidant herbal formulation, which can be used for the treatment of many diseases associated with free radicals generation. [56]

ImmuPlus, a polyherbal formulation contains three medicinal plants *Withania somnifera*, *Tinospora cordifolia* and *Emblica officinali*. This polyherbal formulation was tested for total antioxidant capacity, total reducing power, scavenging activity against DPPH radical and total polyphenol and flavonoid contents by Stefano *et al*. The *in-vitro* study indicates that this polyherbal supplement is a significant source of natural antioxidants which could be helpful in preventing harmful damage by oxidative stress. The strong correlations between antioxidant properties and TPC/TFC in extracts show that polyphenols and flavonoids are major components which are principally responsible for the high antioxidant capacities of the polyherbal formulation. Both of these classes of substances are known for their beneficial effects on health of human and animal beings. [57]

A study was designed to analyse the antioxidant potential of a herbal formulation comprising of *Atrocarpus heterophyllus* Lam (leaves), *Curcuma amada* Roxb (Root) and *Piper longum* Linn (fruits) in paracetamol induced toxicity by Yuvarani *et al*. Wistar

strains of Albino rats were used as the experimental models. The effects of the plant extract on lipid peroxidation (LPO), enzymatic antioxidant-Superoxide dismutase (SOD), Non enzymatic antioxidant-Reduced glutathione (GSH) and protein (tissue and serum) were analysed. The disease control group showed a marked elevation in the LPO levels and a decrease in the protein levels and antioxidant status, which was reversed to near normal in the plant and Liv 52 treated groups. Their study indicated that restoration of the normal functioning of the antioxidant systems in the experimental models through the reduction of lipid peroxidation and increasing the serum and tissue protein levels, which proves that the plants used for the formulation possess antioxidant potentials and are active against paracetamol induced toxicity. [58]

Sitopaladi churna is a reputed Ayurvedic polyherbal medicine consist of five ingredients viz., *Saccharum officinarum* (Sugar candy), *Bambusa arundinacea* (Siliceous concretion), *Piper longum* (dried fruit), *Elettaria cardamomum* (dried seed) and *Cinnamonum zeylanicumm* (Stem bark). Sitopaladi churna was prescribed for pleurodynia, intercostals neuralgia, cough associated with bronchitis, supportive agent for allergy, viral respiratory infection and in pharyngeal and chest congestion. Antioxidant potential of the Sitopaladi churna was studied using different *in- vitro* free radical models like DPPH, ABTS, nitric oxide and superoxide scavenging radical models by Inder *et al*. The polyherbal formulation showed good dose dependent free radical scavenging property in all the models used for the study. The antioxidant potential may be directly linked to the phenolic compounds present in the ingredients of Sitopaladi churna. [59]

Bharagyadi is a polyherbal formulation consisting of three herbs named *Clerodendrum serratum*, *Hedychium spicatum* and *Inula racemosa*, was extensively used in ayurvedic for their antioxidant potential. A work was designed to investigate antioxidant activity of Bharagyadi formulation in search or new, safe and inexpensive antioxidant by Divya *et al*. Hydroalcoholic extract was prepared from the above herbs and was tested for total reducing power and *in-vitro* antioxidant activity by $ABTS^{+}$ assay, Superoxide anion scavenging activity assay and lipid per-oxidation assay. Ascorbic acid was used as standard with IC_{50} value is 4.6µg/ml. The result suggested that Bharagyadi has good potential for antioxidant activity. [60]

Polyherbal formulation having antidepressant activity: RO13, a poly herbal formulation contains *Eclipta alba*, *Glycyrrhiza glabra*, *Hemidesmus indicus*, *Hibiscus rosa-sinensis*, *Nelumbo nucifera*, *Quercus infectoria*, *Rosa damascena*, *Terminalia chebula* and *Zingiber officinalis*. A study was attempted to prove the antidepressant property of RO13, in conventional animal models of depression by Anju *et al*. Albino mice were grouped into four, each group with 6 animals and injected with Normal Saline (control), Imipramine 10 mg/kg (Standard drug), RO13 aqueous extract 200 mg/kg and 400 mg/kg (test drug) orally. The animal groups were subjected to Tail Suspension Test and Force swim test. The results showed that in both Tail suspension test and Force swim test, the aqueous extract of RO13 at the dose of 200 mg/kg and 400 mg/kg significantly reduced immobility time (P<0.01) in acute studies and further reduced in chronic studies. The aqueous extract of RO13 possesses dose dependent antidepressant effect. They concluded that RO13 showed a comparable effect as that of Imipramine in both acute and chronic studies but as RO13 is a polyherbal formulation it is expected to have low side effects. [61]

Polyherbal formulation having CNS depressant activity: Bramhi Ghrita, a polyherbal formulation containing *Bacopa monneri*, *Evolvulus alsinoids*, *Acorus calamus*, *Saussurea lappa* and cow's ghee. The effect of Bramhi Ghrita on motor coordination, behavior, sleep, convulsions, locomotion and analgesia was evaluated in mice using standard procedures by Achliya *et al*. The formulation exhibited reduced alertness, spontaneous locomotor activity and reactivity. It also antagonized the behavioral effects of d-amphetamine, potentiated the pentobarbitone induced sleep and increased the pain threshold. Bramhi Ghrita protected mice from maximum electroshock and pentylene tetrazole-induced convulsions. Bramhi Ghrita also showed antinociceptive action by tail flick method. Bramhi Ghrita inhibited MES and PTZ-induced convulsions in a dose-dependent manner. The study showed that Bramhi Ghrita was CNS depressant with anticonvulsant activities. [62]

Polyherbal formulation having diuretic activity: A study was attempted to investigate the diuretic activity of ethanolic extract of a polyherbal formulation of three drugs *Bryophyllum pinnatum*, *Syzigium aromaticum* and *Ocimum sanctum* by *in-vivo* method by Sarang *et al*. This activity of polyherbal formulation may be attributed to their ability to sparks the excretion of Na^{+}, K^{+} and Cl^{-} concentration in urine along with increase in urinary volume. The mechanism underlying this effect is still unknown, but is apparently related to increased diuresis and lowering of urinary concentrations of calculus promoters, increasing level of calculus inhibitors, antioxidant activity of the flavonoids and change in shape and texture of the urinary stone. [63]

Polyherbal formulation having Anti-bone resorption activity: Yukmi-jihang-tang (YJ) a Korean polyherbal medicine comprised of seven herbs such as *Rehmannia glutinosa*, *Dioscorea japonica*, *Cornus officinalis*, *Smilax glabra*, *Paeonia suffruticosa*, *Alisma platago-aquatica* and *Hominis placenta.* Anti-bone resorption properties of YJ were investigated by Un-Ho *et al*. YJ inhibits *in vitro* and *in vivo* bone resorption by inhibition of phosphorylation of peptide substrates. YJ dose-dependently reduced the hypercalcemia induced in mice by IL-1β and partly prevented bone loss and microarchitectural changes in young ovariectomized

rats, showing that the protective effect on bone was exerted via the inhibition of bone resorption. Their result also suggested that the YJ extracts is effective for bone resorptive action in bone cells. [64]

Polyherbal formulation used in myocardial infarction: Abana is an Indian Ayurvedic herbomineral preparation of selected ingredients, which provides significant protection against ischaemia and hypertension. It's most important plant ingredients are *Terminalia arjuna*, *Withania somnifera*, *Terminalia chebula*, *Phyllanthus emblica*, *Nardostachys jatamansi*, *Tinospora cordifolia*, *Glycyrrhiza glabra*, *Zingiber officinale* and *Nepeta hindostana* etc. To find out the possible role of lipid peroxidation and glutathione in the pathogenesis of myocardial infarction and its protective role a study was conducted by Sheela *et al*. The effect of Abana pretreatment (75 mg/100 g) for a period of 60 days on isoproterenol (20 mg/100 g *s.c.* twice at an interval of 24 hrs) induced lipid peroxidation was studied in rats. Marker enzymes levels such as creatinine kinase, lactate dehydrogenase, alanine transaminase and aspartate transaminase were assessed in serum and heart homogenate. Glutathione content and lipid peroxide levels were also estimated. In isoproterenol administered rats, a significant decrease was observed in the levels of marker enzymes in the heart with a corresponding increase in their levels in serum. Lipid peroxide level measured in terms of "TBA reactants" increased significantly in serum and heart. Abana pretreatment offers significant protection to myocardium against the damage caused by isoproterenol induced lipid peroxidation. [65]

Arogh plus, is a polyherbal formulation manufactured by Rumi Herbals Pvt. Ltd, Chennai, containing *Nelumbo nucifera*, *Hibiscus rosa-sinensis*, *Rosa alba*, *Terminalia chebula*, *Hemidesmus indicus*, *Glycyrrhiza glabra*, *Zingiber officinale*, *Quercus infectoria* and *Eclipta alba*. Arogh Plus, a polyherbal formulation was evaluated clinically in volunteers working under stressful situation by Anoop *et al*. Daily intake of the formulation for a period of continuous 30 days was found to decrease the symptoms observed due to stress, which was reduced and their work performance was found to be increased. All were clinically evaluated based upon symptoms, anthropometric evaluation, hematological, diabetic and serum cortisol and urine profile. All the parameters were evaluated during 0 day, 15th day, 30th day and on 45th day after stopping the drug internally. Three grams of Arogh plus was given twice daily for a period of 30 days was found to decrease symptoms due to stress and the benefits was reinforced by way of significant reduction in serum cortisol with a reduction of 36.99 % within a month. Thus Arogh plus was found to be effective formulation in relieving stress and improving the quality of life. [66]

Polyherbal formulation having anti-cancer activity: Thapring is a Traditional Tibetan Medicine (polyherbal formulation) composed of *Terminalia chebula*, *Saussurea lappa*, *Acorus calamus*, *Aconitum ferox*, *Oxytropis microphylla*, *Commiphora mukul*, *Acacia catechu*, *Delphinium brunonianum* and a mineral ingredient. Evaluation of the pro-apoptotic and anti-tumorigenic properties of Thapring in hepatoma cells and in a transgenic mouse model of hepatocellular carcinoma was done by Tenzin *et al*. The pro-apoptotic action and growth inhibition property of Thapring were assessed in Huh7, HepG2 and A549 cell lines using flow cytometry and MTT assay, respectively. Serological studies for liver function, vascular endothelial growth factor and superoxide dismutase were assessed in the serum of X15-myc transgenic mice. Their study suggested that Thapring possesses a strong anti-cancer activity (growth inhibition, cell cycle arrest, pro-apoptotic activity) in hepatoma cells and shows minimal cytotoxic effect on non-hepatoma cells and nontransformed AML12 hepatocytes. [67]

Polyherbal formulation having anti-HIV activity: In a prospective, single-site, open-label, non-randomized, controlled, pilot trial, was carried out to evaluate an Indian polyherbal formulation (PHF) for its safety and efficacy in treating subjects with HIV-AIDS. A total of 32 and 31 subjects were enrolled under the PHF and highly active antiretroviral treatment (HAART) arms, respectively, and followed up for a period of 24 months. Plasma viral RNA, CD4 cell count and blood chemistry were monitored at 3-month intervals. Following mid-term safety evaluation, 12 subjects from the PHF arm were shifted to HAART and were followed separately as PHF-to-HAART arm, for the rest of the period. In the PHF arm, at 1 month, a significant increase in CD4 cell count and a concomitant decrease in viral load were seen. The PHF appears to have provided protection by delaying the kinetics of CD4 cell reduction. [68]

Study of safety and efficacy of polyherbal formulation (toxicity study): PR-2000 is a polyherbal preparation consists of *Tribulus terrestris*, *Caesalpinia bonducella*, *Asparagus racemosus*, *Areca catechu* and *Crataeva nurvala*. A study was undertaken to evaluate the efficacy of PR-2000, in the treatment of patients with benign prostatic hyperplasia by Shukla *et al*. The trial included 68 patients who were diagnosed with BPH and graded accordingly using the American Urological Association (AUA) symptom score, uroflowmetric study and pelvic ultrasonography to determine the sonographic size of prostate. PR-2000 was administered orally at a dose of 2 tablets thrice daily for six months. All the patients were periodically evaluated for the entire study period. Following six months of treatment, the patients showed encouraging improvement in the AUA score along with an increase in peak flow rate and a subsequent decrease in sonographic size of prostate. No change in biochemical markers was observed and no untoward side effects were noticed during the trial. The results conclude that PR-2000 is an effective, safe and well-tolerated therapy in the treatment of BPH. Almost all the patients began

to show symptomatic relief by the third month of treatment with PR-2000. From the above results it can be stated that PR-2000 is a very effective mode of conservative therapy in patients suffering from benign prostatic hyperplasia. The study also demonstrated that in patients with symptomatic BPH, treatment with PR-2000 is safe since there were no adverse effects. [69]

Amirtha Sanjeevi Kuligai is a a polyherbal formulation prepared by taking *Ferulla asafoedita*, *Costus specious* root, *Electaria cardamomum* fruit, *Syzygium aromaticum* flower bud, *Santalum album* wood, *Picrrorhoea kurora*, *Madhuca longifolia* flower, *Hemidusmus indica* root, *Plectranthus vettiveriodes* root, *Vettiveria zizanoides* root, *Piper longum* fruit, *Glycyrrhiza glabra*, *Cyperus rotundus* root tuber, *Vitis viniferadry* fruit, *Phonex dactylifera* fruit and *Saccharum officinarum* juice. Amirtha Sanjeevi Kuligai (ASK) is prepared as per classical text book of Balavagadam for respiratory problem in paediatric age group. A preclinical study was aimed to find out safety and toxicity of ASK by Sangeetha *et al*. Adult swiss albino rats of either sex of weighing 220- 250 g were used during their study. Acute and Sub-acute toxicity were carried out as per OECD guidelines. Hematological parameters, biochemical parameters, histo-pathological study were performed for all animals. The study concluded that on oral administration of 400 mg/kg of body weight of ASK to swiss albino rats, there was no characteristic clinical sign of toxicity or mortality observed. Based on their finding, no toxic effect was observed up to 400 mg/kg of body weight of Amirtha Sanjeevi Kuligai treated via oral route over a period of 28 days. Thus Amirtha Sanjeevi Kuligai was suitable with the dosage recommendations of upto 400mg/kg body weight *p.o*. [70]

PartySmart is a polyherbal formulation containing extracts of *Phoenix dactylifera*, *Cichorium intybus*, *Andrographis paniculata*, *Vitis vinifera*, *Phyllanthus amarus* and *Emblica officinalis*. Venkataranganna *et al*, was investigated the pharmacodynamics and oral toxicity of PartySmart by taking rats. Effect of PartySmart on blood acetaldehyde and alcohol levels were evaluated at doses of 125, 250 and 500 mg/kg b. wt. in rats. Acute toxicity study was conducted with PartySmart at a test dose of 2000 mg/kg b.wt., *p.o*. In repeated dose with 90 days studies, PartySmart was administered at doses of 500 and 1000 mg/kg b.wt. once-a-day, orally throughout the study period. PartySmart dose-dependently decreased blood ethanol and acetaldehyde levels as compared to control. The LD_{50} of PartySmart was found to be greater than 2000 mg/kg b.wt. No significant differences in PartySmart treated groups were observed on body weight, food intake, haematological and clinical chemistry and organ weight ratios as compared to control group in the repeated dose study. Histopathological examination of all target organs showed no evidence of lesions attributing to drug toxicity. It was also found to be safe and devoid of adverse effects as revealed by toxicity studies. [71]

A polyherbal formulation named TLPL/AY/01/2008 contains husks of *Plantago ovate*, leaf extract of *Cassia angustifolia* and fruits extract of *Emblica officinalis*, *Terminalia chebula* and *Terminalia belerica*. A study was conducted by Raghunatha *et al*, according to current OECD toxicology guidelines for acute and repeated dose. No mortalities or evidence of adverse effects were observed following acute oral gavage administration up to 2000 mg/kg of TLPL/AY/01/2008 in Sprague dawley rats. The 28-day repeated dose study involving daily oral administration of 70, 175 and 350 mg/kg body weight of TLPL/AY/01/2008, with a post trial of 14 days no treatment observation period at high dose level, resulted in no clinical signs and animal deaths. No toxicological significant differences were observed in any of the TLPL/AY/01/2008 treatment groups for body weights, feed consumption, physical appearance, neurological behaviour and urine analysis. Evaluation of haematology and clinical chemistry parameters revealed no toxicological and treatment related effects. No treatment related changes noted in absolute and relative organ weights. Results of their study demonstrated that polyherbal formulation TLPL/AY/01/2008 is not acutely toxic at 2000 mg/kg of body weight/day, with a NOAEL (no-observed-adverse-effect-level) of greater than 350 mg/kg of body weight/day for systemic toxicity from repeated dose 28-day oral gavage administration. [72]

Liv.52 DS Tablet, a polyherbal formulation was prepared by taking eight active medicinal herbs viz., *Capparis spinosa*, *Cichorium intybus*, *Mandura bhasma*, *Solanum nigrum*, *Terminalia arjuna*, *Cassia occidentalis*, *Achilleamille folium* and *Tamarix gallica* by Santanu *et al*. Fifty eligible patients with Non-alcoholic steatohepatitis (NASH) were included in their clinical study. They were instructed to take Liv.52 DS tablets, 2 tablets twice daily for a period of 3 months. The predefined primary endpoints were improvement in steatohepatitis after the administration of Liv.52 DS tablets. The efficacy parameters were improvements in clinical as well as liver function tests, ultrasonographic examination and a non-invasive NAFLD score which evaluates the severity of fatty liver fibrosis. The predefined secondary endpoints were incidences of adverse events and overall compliance to the drug therapy. There were no clinically significant adverse reactions; either reported or observed during the entire study period. The overall compliance to the treatment was good and no treatment discontinuations were reported. The results of their study showed that Liv.52 DS was effective and safe in management of Non-Alcoholic Steatohepatitis. The clinical study clearly shows that Liv.52 DS is beneficial in improving clinical and liver function parameters as well as in Ultrasonographic and NAFLD scores of NASH. There

were no adverse reactions either observed or reported during the study period. [73]

Soshiho-tang (SST, Xiao-chai-hu-tang in Chinese and Sho-saiko-to in Japanese), an oriental herbal formula prepared by taking seven herbs: *Bupleurum falcatum*, *Pinellia ternate*, *Scutellaria baicalensis*, *Zizyphus jujuba*, *Panax ginseng*, *Glycyrrhiza uralensis* and *Zingiber officinale*, used commonly in Korea, China and Japan for treatment of chronic liver diseases. Evaluation of safety of SST in Sprague-Dawley rats over a period of 4-weeks was carriedout by In Sik *et al*. The SST was administered once daily by gavage to male and female rats at doses of 0, 500, 1000 and 2000 mg/kg/day for 4 weeks. The SST treatment did not result in any toxicologically significant changes in mortality, food consumption, ophthalmoscopy, urinalysis, hematology, serum biochemistry, gross pathological findings, absolute/relative organ weights and histopathology, except for salivation and reduction in body weight in the 2000 mg/kg/day male group. The results indicated that SST may be a safe material. The study demonstrated that SST does not induce specific adverse effects in SD rats when used in either sex at doses of up to 2000 mg/kg for 4 weeks. [74]

A study was conducted to evaluate the role of Unani herbal drugs Pepsil and Safoof-e-katira on the gastro esophageal reflux disease (GERD) by Muhammad *et al*. The study was a multicentre randomized case control study conducted at Matab Hakeem Muhammad Noor-ud-din, Burewala; Aziz Muhammad din Medical and Surgical Centre, Burewala and Shifa-ul-mulk Memorial Hospital, Hamdard University, Karachi. The patients were selected according to inclusion and exclusion criteria. In test group-1 the male female ratio was 40%, 60%; test group-2 was 42%, 58% and in control group was 44%, 56% respectively. The statistical results of the study prescribed that all the drugs studied (Pepsil, Safoof-e-katira and Omeprazole) were highly significant. The herbal coded drug Pepsil showed no side effects and unani herbal drug safoof-e-katira showed minimum result of 75% in the patients while Omeprazole resulted with some side effects. Thus the herbal coded drug Pepsil is a potent herbal drug for gastro esophageal reflux disease. Finally it was observed that Pepsil herbal coded medicine has shown superior efficacy as compared to Omeprazole and Safoof-e-Katira because it has not shown any side effects and it is tolerable for all the patients. [75]

Sheng-Fei-Yu-Chuan-Tang (SFYCT) a Traditional Chinese Polyherbal formulation consisting of 13 medicinal plants named, *Panax ginseng*, *Atractylodes macrocephala*, *Citrus reticulate*, *Ephedra sinica*, *Morus alba*, *Bupleurum chinense*, *Cinnamomum cassia*, *Scutellaria baicalensis*, *Schizonepeta tenuifolia*, *Siler divaricatum*, *Glycyrrhiza uralensis*, *Zingiber officinale* and *Zizyphus jujube*, was used to treat patients with lung diseases. A study was conducted by Chia-Hung *et al*, to find out the immunoregulatory effect of SFYCT on intratracheal lipopolysaccharides- (LPS-) challenged acute lung injury (ALI) in mice. Their study showed that SFYCT possesses anti-inflammatory effects in suppressing release of inflammatory cytokines but increasing anti-inflammatory cytokines production. Their results suggested that SFYCT protects against LPS-induced acute lung injury in mice. [76]

A poly herbal formulation (PHF) (dry powder, cream color) was purchased from Chemiloids (manufactures and exporters of herbal extracts; Vijayawada, Andhra Pradesh, India) by Balaji *et al*. Each 5 ml contains different plant materials like *Glycyrrhiza glabra*-70 mg, *Terminalia chebula*-75 mg, *Zingiber officinale*-50 mg, *Cassia senna*-60 mg, *Operculina turpethum*-50 mg, *Asparagus rhacemosus*-55 mg and *Aloe barbadensis*-200 mg. An investigation was done to determine the gastro protective effect of this polyherbal formulation (PHF) at a dose of 150 mg/kg in a model of aspirin induced ulcers in rats and to study the mechanism involved using H_2 receptor blocker Ranitidine as comparison. In treated groups of animals the *in vivo* antioxidant levels such as SOD, CAT and glutathione levels were increased and LPO levels was decrease and found more or less equal to the normal values. The histopathological examinations of the stomach of the ulcerated animal's show severe erosion of gastric mucosa, submucosa edema and neutrophil infiltration. These results suggested that the gastroprotective effects of PHF in this experimental model through antioxidant and cytoprotective activity. [77]

Exher a polyherbal formulation contains *Aloe vera, Convolvuls microphyllus*, *Saraka ashoka*, *Tribulus terrestris*, *Hemidesmus indicus*, *Trigonella foenum-graecum*, *Symplocos racemosa*, *Cyperus rotundus* and *Asparagus racemosa.* Exher was evaluated for its oestrogenic effect using *in-vivo* and *in-vitro* experimental models by Hanumantharayappa *et al*. Oestrogenic effect of Exher-1 (250 mg/kg *p.o.*) & Exher-2 (500 mg/kg *p.o.*) were studied in normal and ovariectomized rats. Exher-1 & Exher-2 were administered as an aqueous suspension for a period of 21 days. The effect of Exher-1 (250 mg/kg *p.o.* for 21 days) & Exher-2 (500 mg/kg *p.o.* for 21days) was also studied on normal rats for regular oestrus cycle. *In-vitro* studies with Exher (50-400µg/ml of aqueous extract) on isolated uterus in non-gravid, non-oestrinised rats were carried out to find out whether the formulation possesses any oxytocin like activity. Administration of Exher-1 in normal rats significantly increased the dry uterine weight but not the wet uterine weight. It also resulted in marked increase of oestrogen levels with no change in progesterone levels as compared to control. Administration of Exher-2 in normal rats has failed to significantly increase the dry and wet uterine weight. Exher-1 and Exher-2 treatment in ovariectomized rats did not show any increase in uterine weight and oestrogen concentration. The rats from both control and treated group showed normal oestrus cycle. Aqueous

extract of Exher had no significant effect on the *in-vitro* acetylcholine-induced contraction and uterine motility. Exher possess oestrogenic activity only in the presence of functional ovary and is devoid of any progestational activity. Exher is capable of preventing and curing uterine fibroids and abnormal uterine bleeding only in the presence of functional ovary. It is found to be ineffective in case of non-functional ovary. The Exher can be used in conditions like menstrual irregularities as it was found to be safe on rat oestrus cycle by maintaining the regular oestrus cycle. [78]

In the developing countries increased cost of medicine as well as their side effects has become a great task when the public health is concerned. Investigations have been carried out from time to time to develop different types of polyherbal formulations to enhance the overall therapeutic potential of the formulation. In this review, we have presented information about various polyherbal formulations, their pharmacological properties along with their toxicity studies which will be helpful for further investigation of other therapeutic potential and mechanism of action of these polyherbal formulations.

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