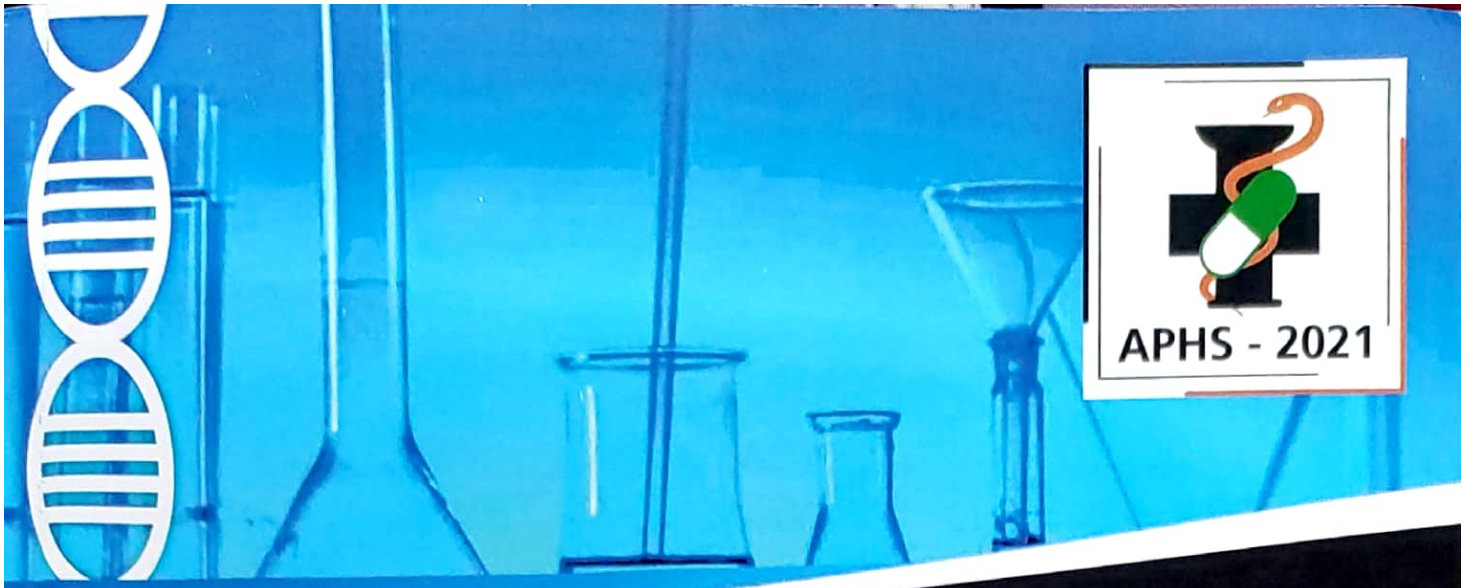

APHS - 2021

Advances in Pharmaceutical and Health Sciences

Edited by

K. Nagarajan, Vaishali M. Patil, AB Pant

Vinay Kumar, Abhishek Kumar, Praveen Kumar Dixit

Anjleena Malhotra, Shipra Singhal

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Advances in Pharmaceutical and Health Science

PREFACE

International Conference on Advances in Pharmaceutical Health Sciences (APHS) was organized by KIET School of Pharmacy, KIET Group of Institutions, India in collaboration with CSIR-Indian Institute of Toxicological Research, Lucknow, India on 7th and 8th October 2021. Eminent researchers from international and national institutes of repute have delivered keynote sessions on emerging technologies and advents in the field of pharmaceutical and health sciences. Research manuscripts were received from different parts of the country which were selected after peer review and were accepted for publication in the form of book chapter. All the authors/contributors of the chapter gave their best to make this book.

The book chapters are covering the wide spectrum of technological and process advances in drug delivery, analytical method development, isolation and evaluation of phytoconstituents, computer-aided drug design, pharmacology, devices used in health care and food science. Anti-COVID therapeutics is also the topic of interest for some chapters as per the current demand of pharmaceutical industry.

The readers could explore and offer updates of recent developments and present the latest results from their studies. Various eminent themes, targeted towards artificial intelligence in health care, attracted rich diversity of authors from various universities and industries around the globe to discuss the most recent innovations, trends and concerns in the field of science and technology.

Editors

ACKNOWLEDGEMENT

Truly we believe the International Conference on "Advances in Pharmaceutical and Health Sciences" has played an eminent role in providing us a great scope for learning innovative ideas and inventions and it has also strengthened our bonding with a number of eminent personalities. On behalf of the Organizing Committee of the International conference, we are pleased to share that it was an extremely enriching and successful event. It has been a feeling of pride and privilege to serve as editor of this book.

First and foremost, we extend our heartfelt thanks to God for his grace in making our conference successful. We are grateful to the members of the international and national advisory committee, collaborators and guests for the conference for their contributions and suggestions. We extend our deepest gratitude to the Chief Patron (APHS-2021) and Shri. Sarish Agarwal, Honorable Chairman, Governing Council, KIET Group of Institutions, for his motivation and blessings. Our sincere thanks to the Patron, Dr. (Col.) A. Garg (Director, KIET Group of Institutions, Ghaziabad) and Dr. S. K. Barik (Director, CSIR-Indian Institute of Toxicology Research, Lucknow), and Co-Patron, Dr. Manoj Goel (Joint Director, KIET Group of Institutions, Ghaziabad) and Dr. Anil K. Ahlawat (Dean Academics, KIET Group of Institutions, Ghaziabad) for their guidance and moral support. We humbly acknowledge the excellent support of the technical collaborator CSIR-Indian Institute of Toxicological Research, Lucknow, India for the collaborative contribution towards the grand success of APHS-2021. Special thanks to the contributing authors, delegates, and reviewers for their vital contribution through excellent papers. We are pleased to acknowledge the hard working and efficient brains behind this conference, the Organizing Committee members of (APHS 2021). We humbly acknowledge Mr. Vinay Ahlawat and ITSS team for their support. We even recognize all those who contributed directly or indirectly to publish this book.

Prof. (Dr.) K. Nagarajan
Dr. Vaishali M. Patil
Dr. AB Pant
Dr. Vinay Kumar
Dr. Abhishek Kumar
Dr. Anjleena Malhotra
Ms. Shipra Singhal

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FORMULATION AND PRE-COMPRESSIONAL STUDIES OF POLYHERBAL GRANULES OF *CUMINUM CYMINUM* AND *TRIGONELLA FOENUMGRAECUM* FOR HYPERLIPIDEMIA

Shivangi Singh[1], Dhairya Agarwal[1], Deepak Gupta[1], Neeti Srivastav[2]*and Anita Singh[2]

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Abstract

The utilization of natural products for their pharmaceutical and nutraceuticals purposes have high value in prevention and treatment of myriad illness. Nutraceutical is a food or apart of food that provides health benefits in the terms of both prevention and treatment of disease.In recent years the consumers have started to look forward to food as a basic nutritional source. Food is thus used as a factor for health promotion beyond its nutritional value. In pharmaceutical industry, the formulation of natural products into an effective and stable dosage form necessitates evaluation of the processing techniques required and the properties of the product obtained. The objective of the present study was to prepare and evaluate *Cuminum cyminum* and *Trigonella foenumgraecum* granules to develop solid dosage forms. Cumin (*Cuminum cyminum*) is a herbaceous plant belonging to Apiaceae family known as Zeera whereas Fenugreek, (Trigonella foenumgraecum), also spelled foenugreek, is a fragrant herb of the pea family Fabaceae. *Cuminum cyminum* and *Trigonella foenumgraecum* seeds were dried and grinded into fine powder. Dried powdered of Cumin and Fenugreek seeds were granulated by using starch paste as a binder. The prepared granules were evaluated for different parameters including- angle of repose, bulk density, tapped density, hausner index and Carr's index The influence of Glidant concentration on the granule properties were also investigated.

Keywords: Wet granulation ,Nutraceutical, Flow properties, Glidant.

Introduction

Formulations composed from the plants or its parts are an important source in curing diseases. Most of these formulations do not adhere to the basic principles to be followed in the production of such traditional dosage forms which may lead to serious hazards. So, in recent years the consumers have started to look forward to food as a basic nutritional source. Food is thus used as a factor for health promotion beyond its nutritional value. Tamilvanan S et.al.(2006) & Chauhan B, et al (2013) described nutraceutical is a food or apart of food that provides health benefits in the terms of both prevention and treatment of disease.

According to Deng R A et al (2012) & Suresh C.V et al(2020) nutraceutical has changed the traditional dividing line between food and medicine and thus termed as Functional Food. The most common advantages to rely on plant products are: Availability; Affordability; Safety; No side effect

Cumin (*Cuminum cyminum*) is a herbaceous plant belonging to Apiaceae family known as Zeera. It is used as Antifungal, Anti-inflammatory, Anti oxidant, Anti diabetic, Hypolipidemic, Anti epileptic and in jaundice.Hyperlipidemia is a medical as well as social problem that has morbidity and mortality. The major risk factors include- atherosclerosis that gives rise to Ischemic heart disease and CV disease studied by Moosa AS et al (2005) Fenugreek leaves and seeds have been used extensively to prepare extracts and powders for medicinal uses Ethan Basch et al (2003) .Fenugreek isreported to have anti-diabetic, anti-fertility, anticancer,anti-microbial, anti-parasitic and hypocholesterolaemic, effects Ramya Premanath et al (2011), Hypocholesterolaemic effect Joanna S et al (2003) & KavithaVenkatesan et al (2003).Oral route has been one of the most popular routes of drug delivery due to its ease of administration, patience compliance, least sterility constraints and flexible design of dosage forms.Granulation is the process of particle enlargement where fine particles are changed to larger ones as granules or agglomerates SrinivasanShanmugam et al (2015). It is the most significant operation for the production of pharmaceutical dosage forms, mostly tablets and capsules.

Hyperlipidemia is increase serum total count (TC), triglycerides (TG), very low-density lipoproteins (VLDL), Low-density lipoproteins (LDL) and (intermediate density lipoprotein (IDL) which are responsible for various complications like: heart attack, premature coronary artery disease, stroke, atherosclerosis, myocardial infarction and pancreatitis Tamilvanan S et al (2006). It is expected that the cardiac diseases are the leading cause of death and disability worldwide Chauhan B et al (2013) . Atherosclerosis and atherosclerosis - Associated conditions such as coronary heart diseases (CHD), ischemic cerebrovascular disease, and peripheral vascular diseases are due to increase lipid count in the serum. Plants having medicinal values play an important role in the health care from ancient age. Approx. 80% of the world population believes on the use of traditional medicine which are predominantly based on plant/herbal materials RamyaPremanath et al (2013) . If we talk about the granules they are widely

accepted as they offer an advantage of faster disintegration and dissolution, palatability, greater acceptance among pediatric and geriatrics. They are considered as more economical.

MATERIALS AND METHOD

Materials

Fenugreek seeds and Cumin seeds: were purchased from local market of Ghaziabad.
Lactose (Fischer Scientific), Sodium CMC, Talc, Magnesium stearate (Qualikem),Starch (Rankem) was purchased from India.

Method

Cumin seed and Fenugreek seeds were properly cleaned with water and completely dried in open air. It was finally powdered in the mechanical grinder and passthrough sieve no 40 along with the other ingredients. Starch paste of 20% concentration was prepared and mixed in the powder mixture as binder for preparation of granules. The wet mass was passed through sieve number 10 to obtain the granules. The prepared granules were dried at 40^{O}C in tray dryer.

Evaluation of Nutraceutical granules

For developing any dosage form, preformulation study is the prior step in the potential drug development. One of the basic process is to study pre compressional parameters like- angle of repose, bulk density, tapped density, compressibility indices etc.

Angle of repose

Lachman L et al (2015) & Kushwaha A et al (2018) The angle of repose was determined by allowing the powder to free flow through a funnel on to the surface. Further addition of powder was stopped as the pile touched the tip of the funnel. The rough circle was drawn around the pile without disturbing it. The height and diameter of resulting cone/pile was measured. The same procedure was repeated three times to get average value.

Angle of repose was calculated by using the following equation: **Tan 0 = h/r**
Where, h = Height of the powder cone; r = Radius of the powder.

Bulk density

Lachman L et al (2015) A sufficient quantity of material was passed through a sieve no.18. Then take 100 gm of powder and filled it into a dry 250 mi of masuring cylinder . Than level of powder was adjusted without compacting and the apparent volume (Vo) was noted. Bulk density was calculated, in g/ml using the formula: **Bulk density = M/Vo**
Where, M = Mass of the powder cone, V0 = Apparent volume of powder.

Tapped density

Accurately weighed quantity of powder was filled into a measuring cylinder. Then sample was tapped by raising the cylinder and allowing it to drop under its own weight using a suitable mechanical tapped density tester at a nominal rate of 300 drops/min. The cylinder was tapped 500 times to measured the tapped volume (Va). The Procedure was repeated for an additional 750 tapings and again the tapped volume was measured as (Vb). If the difference between Va and Vb was <2%, Vb was the final tapped volume (Vf) . If the difference was higher, the tapings were repeated for an additional 1,250 times, and then the tapped density was calculated using the formula given below:
Tapped density = M / Vf
Where, M =Weight of sample taken ,Vf = Final tapped volume

Compressibility Indices

Carr's index

The compressibility index of granules was determined using Carr's compressibility index, as-

$$\text{Carr's index} = \frac{(\text{Tapped density} - \text{Bulk density}) \times 100}{\text{Tapped density}}$$

Hausner's ratio (Bhope SG et al 2011)
The Hausner's ratio was determined using the following formula:
Hausner's ratio = Tapped density / Bulk density

Table No.1: Angle of repose as an indication of granules flow property (Indian Pharmacopoeia 2010)

Angle of Repose	Type of flow
<20	Excellent
20–30	Good
30–40	Passable
>40	Vary Passable

No. 2: Carr's index as an indication of ganules flow. Athawale RB et al **(2011)**

Carr's index (%)	Flowability
5–15	Excellent
12–16	Good
18–21	Fair to passable

23–35	Poor
33–38	Very poor
>40	Extremely poor

Table No.3: Hausner's ratio. Athawale RB et al (2011)

Hausner's ratio	Flowability
<1.25	Good
>1.25	Poor

MATERIALS AND METHOD

Table No.4: Formulation Table

Ingredients (in mg)	Granules F1	Granules F2	Granules F3
Fenugreek seeds powder	50	50	50
Cumin Powder	50	50	50
Lactose	231	226	221
Sodium Sachrine	1.5	1.5	1.5
Talc	-	3.5	7
Magnesium Stearate	-	1.5	3
Starch	17.5	17.5	17.5
Total Weight	350	350	350

Method

Nutraceutical granules containing Fenugreek & cumin seeds powder were prepared by wet granulation method. Other ingredients like lactose was used as diluent, magnesium stearate as lubricant and talc as glidant. All the excipients along with API weighed as shown in Table 1 and passed through sieve no. 20. Then, all ingredients were mixed excluding glidant and lubricant thoroughly for 15min. The powder blend was thoroughly mixed with talc and magnesium stearate .

RESULT

Pre-compressional parameters of granules were studied like angle of repose, bulk density, tapped density, compressibility indices etc. It was found that the lowest angle of repose was observed in F2 formulation. In the same way other parameters like Bulk Density, Tapped Density, Carr's Index and Hausner's Ratio were also found to be lowest indicating higher porosity and an excellent flow. Angle of repose was found to be more than 30^0 in the formulation F1 where no glidant and lubricant was used, indicating poor flow as compared to formulations F2 and F3.

Table No.5: Pre-compression studies of nutraceutical granules.

Pre-Compression Parameters	Granules without adding Glidant and Lubricants (F1)	Granules with Glidant and Lubricants	
		Granules (F2)	Granules (F3)
Angle of Repose (^{0})	32.6	28.88	29.75
Bulk Density(g/ml)	1.20	1.17	1.19
Tapped Density(g/ml)	1.35	1.34	1.37
Carr's Index	11.1	13.4	13.1
Hausner's Ratio	1.12	1.14	1.15

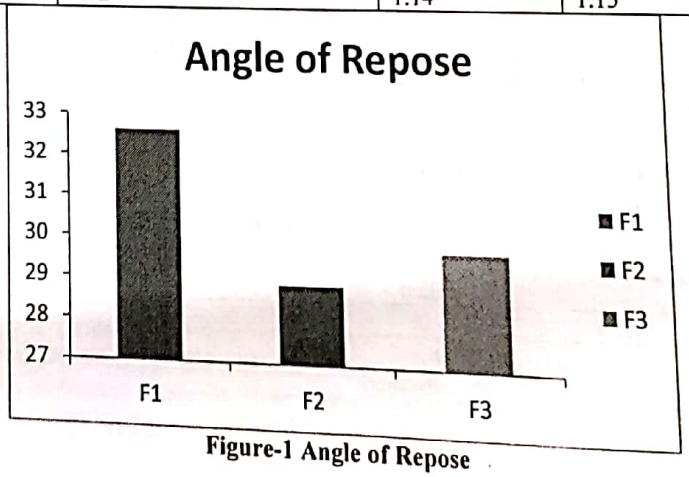

Figure-1 Angle of Repose

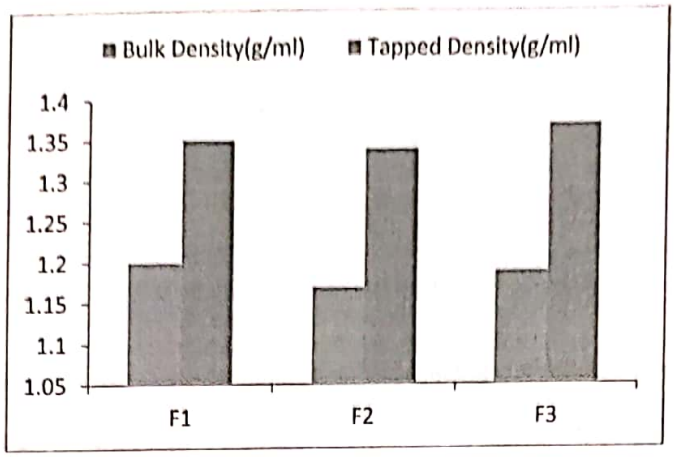

Figure-2 Bulk Density

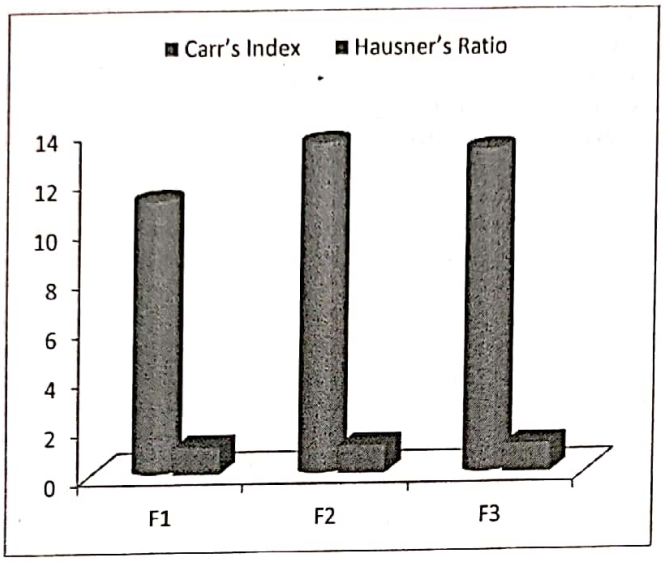

Figure-3 Carr's Index and Husner's Ratio

Conclusion: From the above pre compressional study, we conclude that the nutraceutical granules of Fenugreek seeds and Cumin seeds prepared by wet granulation method gave satisfactory and acceptable results. It concludes that Granules F2 possess good flow properties and can be applied and used as a suitable formulation for nutraceutical granulesand tablets.

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ROLE OF NUTRACEUTICALS AS FOOD AND A MEDICINE

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ABSTRACT

Nutraceuticals are food or part of food comprised of bioactives that impart physiological as well as medicinal effects to maintain the human health and in preventing many acute and chronic diseases. They are the oral dietary supplements that are naturally found in food and possess health benefits. Various food products like prebiotics, probiotics, dietary fibers, fatty acids (polyunsaturated) antioxidants, spices, herbs, nutrients and dietary supplements are a part of it. The sources of nutraceuticals might be chemical, herbal extracts, phytoconstituents or minerals. The purpose of designing nutraceuticals is to improve physical health along with safety by reducing deleterious effects of medicines. Therefore, nutraceuticals help in providing the necessary nutrients and are taken or prescribed based on the requirements. The nutraceuticals are primarily used for the prevention of various diseases such as Obesity, Cardiovascular Disease (CVD), Cancer, Osteoporosis, Arthritis, Parkinson's disease, increased sugar and cholesterol level etc. It may delay aging and increase life expectancy. The current review provides information regarding the status of nutraceutical along with its classification, advantages, limitations, regulatory aspects, role in the prevention of diseases and for other health benefits. Nutraceuticals have attracted interest towards the market due to its proper potential nutritional values, safety and therapeutic effects.

Keywords: *Nutraceuticals, Functional Foods, Phytoconstituents, Herbals, Diabetes, Cancer*

INTRODUCTION

The term nutraceutical is not new has been adopted many years back. An attempt was made in United States for creating a functional component through fortification by adding iodine to salt in order to prevent goitre, representing one of the novel tasks. If we talk in the terms of marketing,"Nutraceutical" has been developed as nutritional supplement and sold in the market with an intention to treat or prevent disease. Therefore, we can say that a "nutraceutical" can be considered either a food or it's part. They have a broader range, starting from isolated nutrients to dietary supplements and even genetically engineered "designer" foods, processed foods and herbal product. Nutraceuticals play a potential role in the betterment of health. it even delays the aging process, give protection from chronic diseases, it increases expectancy of life. Nutraceuticals are the substances that are usually not patent protected but used to prevent diseases. Apart from the nutrition these substances are used for health purposes. Currently over more than 470 nutraceuticals as well as functional food products exists with reported health benefits[2].

Thus, as far as definition is concerned, we can say that a "nutraceutical" is entire food or it's part that benefits us in two aspects, one medically and in other in terms of health, thereby used for the prevention of diseases[3]. So, if we talk about its advantages, they are

ADVANTAGES OF NUTRACEUTICALS

1. Nutraceuticals help to prevent diseases.
2. Helps consumers to fulfill the daily dose requirements of vitamins and minerals.
3. In comparison to conventional pharmaceuticals, these are less toxic.
4. They are cost effective and easily available.

LIMITATIONS OF NUTRACEUTICALS

Nutraceuticals are easily available and does not require prescription. These are considered as food, not a drug. Food laws regulate the quality and manufacturing processes. The major limitations are

1. Presence of adulterations due to the lack of pharmaceutical quality control.
2. The purity and dosage of the nutraceuticals is ambiguous.
3. Cost is another cause of concern in its production.

According to European Medicines law a nutraceutical can be included in the category of medicine for two reasons:

1. It can be used for the prevention, treatment and cure of a condition or disease
2. It can be administered in order to restore, correct or modify the physiological functions in human beings[4].

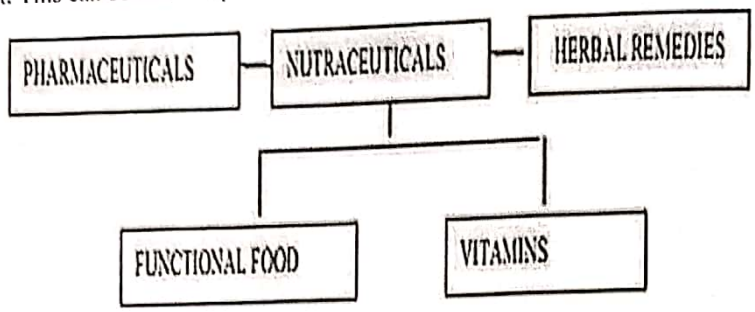
CLASSIFICATION OF NUTRACEUTICALS: There are many ways so as to classify nutraceuticals like

1. Availability of scientific data
2. The source of food
3. According to the mechanism of action
4. Based on chemical nature

Broadly nutraceuticals can be classified as:

1. Potential nutraceuticals
2. Established nutraceuticals

A potential nutraceutical is one that gives good health or medical benefits. A potential nutraceutical comes under the category of established one after having sufficient clinical data to demonstrate its benefits[5]. Most of the nutraceutical products come under the category of potential one due to lack of literature availability. The food products that fall under the category of nutraceutical are Probiotic, Prebiotic, Dietaryfiber, Omega 3 fatty acid and Antioxidant. This can be better explained with the help of the flow chart of nutraceutical classification



Nutraceuticals can be studied under the following three broad categories[6]

- **Nutrients** –These are the substances that have established nutritional functions whichinclude vitamins, minerals, amino acids and fatty acids
- **Herbals** –These are the concentrates and extracts of herbs and other botanical products.
- **Dietary supplements**–These include reagents derived from other sources like steroid hormone precursors, pyruvate, chondroitin sulphate that serve specific functions like as nutrition for sports, weight loss supplements and replacements for meal.

NUTRIENTS

This includes prebiotics, probiotics, dietary fiber, fatty acids that are polyunsaturated in nature, various natural antioxidants. Most of the nutraceutical products come under the category of potential ones due to lack of literature availability.

HERBALS

Since ancient times, herbs have been used as natural remedies for curing many disorders. According to the traditional medicinal system, herbs have innate abilities to treat illness and serve mankind. Various researches related to the biological activity and toxicity of chemical components present in herbs have been carried out.

- **Herbals/ Phytochemicals:** include herbs and botanical products.

Aloe vera: it is used as an anti-inflammatory, emollient and wound healing.

- **Evening Primrose oil:** it plays an important role in treating atopic eczema and also act as a supplement for linoleic acid.
- **Garlic:** It is used as antibacterial, antifungal, antithrombotic, anti-inflammatory like allicin.
- **Ginger:** It is used as a carminative, antiemetic and in the treatment of dizziness.
- **Ginseng:** It is an adaptogen.
- **Green tea:** It is important for boosting up both types of immunity – humoral as well as cell mediated. It is also a potent antioxidant.
- **Others:** Herbs that may include vegetables, fruits, whole grain, nuts and various seeds may contain phenolic compounds, sulphur compounds, pigments other phytoconstituent like terpenoids etc.

VITAMINS

These come under the category of dietary supplements, that contain nutrients derived from food products. The ingredients present in these products include metabolites, vitamins, minerals, herbs, and amino acids.

FUNCTIONAL FOODS

These are the enriched foods that are available in their original form to the consumer. The enrichment of food is called Nutrification. They fulfill the need of various nutrients like vitamins, carbohydrate, fat, proteins to body. The characteristic features of functional food include-

1. should be in their naturally occurring form,
2. should be one of an essential part of our daily diet,
3. should regulate a biological process to prevent disease.

DIETARY FIBER

Dietary fiber can be called as roughage or bulk. Roughages are the plant parts that are difficult for the body to digest. Fats, proteins or carbohydrates can be broken down and absorbed, but fiber can't be digested by the body, rather passes as such through GIT and then finally gets eliminated. Dietary fiber is present in abundance in

fruits, vegetables, legumes and whole grains. It is very essential to prevent or relieve constipation. Fiber can be differentiated into two- soluble and insoluble form[7].

PHYTOCHEMICALS

The constituents that are bioactive and help to build up health are called as Phytochemicals. They are in much demand in pharmaceutical industry. Various forms of food like beans, grains, vegetables are rich source of phytochemical and thus serve as a potential nutraceutical. The term phytochemical emphasizes the plant source of some of the health-protecting compounds. The terms "phytochemical" and "phytonutrient" can be interchanged for describing the active components of plants. They have antioxidant, immune-boosting and other health-promoting properties of active compounds. They may include terpenes, carotenoids, limonoids, and phytosterols.

ROLES OF PHYTOCHEMICALS

1. They are a substrate for various biochemical reactions.
2. They act as a cofactor of enzymatic reactions.
3. They are the inhibitors of enzymatic reactions.
4. They are used as an absorbent thereby bind and eliminate the undesirable constituents in the intestine.
5. Helps to increase the absorption and stability of essential nutrients.
6. They act as a selective growth factor for beneficial bacteria.
7. They destroy intestinal bacteria that are harmful.
8. Act as scavengers.

ROLE OF NUTRACEUTICALS IN PREVENTION OF DISEASES Nutraceuticals and cardiovascular diseases

Components like- anti-oxidants, dietary fibers, Omega-3 poly-unsaturated fatty acids, minerals, vitamins, are used for the prevention and treatment of Cardio vascular disease. In grapes, polyphenol is present that prevents and controls arterial diseases.

In onion, grapes, red wine, apples, and cherries, flavonoids are present that block the Angiotensin enzymes and give strength to those small capillaries that are responsible for the transport of oxygen and nutrients to all cells.

Rice bran lowers the level of serum cholesterol in the blood, thus helps in the reduction of the level of bad cholesterol (LDL) and increases the level of good cholesterol (HDL). Rice bran contains Lutein and Zeaxanthin, that helps in improving vision and reduces the possibility of cataracts. Other components of rice bran important for eye health are omega-3, omega-6, omega-9 and folic acid.

More mortality in CVD is observed with low intake of fruits and vegetables[8].

Diseases associated with diet

In today's scenario the incidence of diet-related diseases are progressively increasing due to more intake of high caloric food and a sedentary lifestyle. Various diseases related to the diet are- increased sugar level, over weight, degeneration of nerve and atherosclerosis.

Heart attack and lung cancer

Corn contains high quantity of fiber and folates. Corn maintains the homocysteine, whose high level is directly responsible for the damage of blood vessels, heart attack, stroke, or peripheral vascular disease. It has been observed that if folate be consumed 100% of daily value, then it may reduce chances of heart attacks by 10%.Cryptoxanthin which is a natural pigment, is one of the components obtained from corn reduces the occurrence of lung cancer.

Obesity

Obesity is a problem across the globe and is defined as accumulation of unhealthy and extra amount of body fat. It gives rise to various risk factors like CHF, angina pectoris, rise in blood pressure, disorders of respiratory system, thrombosis of renal vein, osteoarthritis, formation of cancerous cells, hyperlipidemia, and reduced fertility.

Diabetes

Lipoic acid, an antioxidant is used for treating diabetic neuropathy. Dietary fibers from psyllium are used to control sugar in diabetic patients and also reduces lipid levels in hyperlipidemia cases.

Cancer

Flavonoids prevent estrogen-induced cancers by blocking the enzymes producing estrogen. They may even prevent prostate/breast cancer. Soy-foods curcumin from curry and soya isoflavones possess cancer preventive properties. Lycopene gets accumulated in the skin, testes, adrenal and prostate where it protects against cancer.

Anti-Inflammatory

Curcumin which is a polyphenol of turmeric possesses anti-carcinogenic, antioxidative and anti-inflammatory properties. Anti-tumor activity is found in beet root, cucumber, spinach leaves, and turmeric rhizomes. For the

treatment of auto immune diseases and for reducing inflammation, Gamma linolenic acid is used which is present green leafy vegetables and also in the oils obtained from vegetables (evening primrose oil, blackcurrant and hemp seed oil). Glucosamine and chondroitin sulfate are used to prevent osteoarthritis.

Parkinson's disease

Vitamin E present in the food is important in order to prevent Parkinson's disease. Even creatine may modify Parkinson's disease. Significant results were obtained in preliminary studies done for nutritional supplements. Still due to insufficient scientific data it is not recommended for Parkinson's disease at present.

Osteoarthritis

Osteoarthritis (OA) is a major form of joint disorder. Individuals having pain in joints due to OA and other joint disorders may experience reduced physical activity resulting in weight gain. The weight gain put additional stress on joints. Osteoarthritis is prevented with the use of chondroitin sulfate (CS) and glucosamine (GLN).[9]

Adrenal dysfunction

Adaptogens are the plants that are non toxic and help body to resist various stressors like physical, chemical or biological. Their use in Chinese and Ayurvedic traditions were explained long years back. Adaptogens include herbs *Eleutherococcus senticosus*, *Ocimum sanctum*, *Ginkgo biloba, Panax ginseng* and, *Withania somnifera* and the mushroom *Cordyceps sinensis*. Following is a short description of each.

Chinese have been using *Ginkgo biloba* for last so many years in various indications like vertigo, short-term memory loss, attention or vigilance loss. They have antioxidant and neuroprotective properties, including slowing the progression of dementia.

Ocimum sanctum called as Holy basil or tulsi is used in Ayurvedic medicine and has been shown to relieve from stress .Sembulingham et al. subjected rats to noise stress, with and without *Ocimum* administration. The rats that have been administered with *Ocimum*, were found to have a significantly reduced levels of corticosterone irrespective of the noise stress. The prominent roles of nutraceuticals are explained in a nut shell in the tables given below[10]

REGULATORY ASPECT:

Nutraceutical market is governed by the Dietary Supplement Health and Education Act

(DSHEA) passed in 1994. Food Safety and Standard Authority regulates the registration procedure of food industry as well as its licensing, packaging and storage. A state of confusion exists in the regulator's mind regarding the misconception in the difference between functional food and nutraceuticals. This is the reason of introducing Food Safety and Standards Act that can make our country ready for the global competition. [61]

CONCLUSION:

The aim of the topic is to get a better insight of the potential benefits of the nutraceuticals, their advantages like improving health, to delay the aging process, prevent chronic diseases and thus increasing the life expectancy. In a nut shell we can say that they serve as a support for the body. Even during pandemic conditions prevailing in the country, the market for nutraceuticals remained in the growth phase. It acts as an immunity enhancer that gives power to get protected from different diseases and therefore due to its multipurpose role, it has attracted many companies globally to enter into this business so that this field can flourish well in near future.

Table 1: Roles of Nutraceuticals

Physiological property	Proposed effect	Health benefits
Soluble dietary fiber	Gastric emptying is delayed and prolongs the intestinal phase	Safety contribution
	Nutrients uptake in small intestine is delayed	Lower down the blood cholesterol level[11].
	Prevent the reabsorption of bile acid	Protects against breast cancer
	Prevent the digestive enzymes from reaching lipid substrates, inhibits enzyme activity	Lowers glucose, insulin (Type II diabetics)[13] and lipid level after meal.
Interaction or binding	Binds with bile acids	Lower blood cholesterol level.
	Fermentation	Interacts with digestive enzymes
		Growth of health promoting bacteria
		Short chain fatty acids are

Lowers glucose, insulin and lipid level after meal.	Act as anti-inflammatory and protects against colorectalcancer[14].	Lower down the blood cholesterol level and protect against cancer. 15
	produced	Reduce the incidence of colorectal cancer and intestinal diseases.
	Increase stool weight[16]	Reduces absorption time for nutrients and lowers the level
Insoluble dietary fiber		of glucose, insulin and lipid
	Transit time is speed up	

Table 2: Role of Nutrients in providing health benefits

Nutrients	Health benefits
Fat Soluble Vitamins	
Vitamin A	Effective antioxidant, required for the growth and development, keeps eyes, mucous membrane and the skin healthy, also helps in the prevention and treatment of certain cancers and skin disorders[17].
Vitamin D	Required for the formation of bones and teeth and helps in the calcium absorption[18]
Vitamin E	Acts as an antioxidant and helps in the formation of blood cells, muscles, lung and nerve tissue[19], it is immune system enhancer
Vitamin K	It is essential for blood clotting and helps in wound healing[20]
Water Soluble Vitamins	
Vitamin C	Prevents common cold[21]
Vitamin B1	Essential in neurologic functions[22]
Vitamin B2	Helps for producing energy to perform other chemical processes in the body, helps to maintain healthy eyes, skin and nerve function. Helps in the conversion of food into energy and thus maintain proper brain function[23]
Vitamin B3	Helps in the production of essential proteins[24] and its conversion into energy.
Vitamin B6	Helps in the production of genetic material of cells, helps to form red blood cells[25] it synthesizes amino acids and is aids in metabolism of fats[26], protein and carbohydrates[27].
Vitamin B12	Genetic materials of cells are formed, required during the first trimester of pregnancy to prevent birth defects[28], helps in RBC formation, protects from cardiac diseases
Folic acid	Required for the steroid, cholesterol and fatty acids synthesis[29]also important for intra-neuronal synthesis of acetylcholine
Pantothenic acid	
Minerals	
Calcium	Plays a vital role for building bones and teeth thus maintaining its strength, also important for nerve, muscle and glandular functions[30]
Iron	Important for the production of energy and helps in the

	transportation of oxygen to tissues[31]
Magnesium	Essential for healthy nerve and muscle function and bone formation, may help prevent premenstrual syndrome (PMS)[32]
Phosphorous	Important constituent for building healthy bones and teeth, helps in formation of genetic material[33], produces energy and even stores it.
Trace elements	
Chromium	Helps in the conversion of carbohydrates and fats into energy[34]
Cobalt	One of an essential component of vitamin B12, cobalt when ingested is metabolized *in vivo* for the formation of B12coenzymes
Copper	Important constituent for the production of hemoglobin and collagen[35], helps in proper functioning of the heart, produces energy, helps in the absorption of iron from digestive tract[36]
Iodine	Required forthe proper functioning of thyroid[37]
Selenium	Essential for proper functioning of the heart muscle[38]
Zinc	Plays a significant role in cell reproduction, provides normal growth and development in children, wound healing, aids in the production of sperm and testosterone[39]
Biotin	Needed for various metabolic functions
L- Carnitine Choline Vitamin F ~~Inositol~~ Taurine	Required for the oxidation of fatty acids[40], promotes certain organic acid excretion and even the rate of oxidative phosphorylation is increased It is a lipotropic agent which is used to treat fatty liver[41] and in the conditions of disturbed fat metabolism Required for the proper development of various membranes, responsible for the synthesis of prostaglandins[42],leukotrienes and different hydroxyl fatty acids Being a lipotropic agent, it is necessary for the transport of amino acid and movement of potassium andsodium[43] Helps in bile acid conjugation, photoreceptor activity of retina, white blood ~~cell formation, act as CNS neuromodulator, for platelet aggregation, cardiac~~ contractility, sperm motility[44] also

act as an antioxidant[45]

Table 3: Phytochemicals and their uses

Chemical constituents	Uses
Carotenoids	
Lycopene	They reduce cholesterol levels, antioxidants, protects against cancer[46]
β-Carotene	Antioxidants, protection of cornea against UV light[47]
Lutein	Protect eyes against age related muscular degenerations[48], cataracts, anticancer activity(colon)
Tocotrienol	Improves cardio vascular health, fight against breast cancer[49,50]
Saponins	Very effective against colon cancer[51], reduces cholesterol level
Polyphenolic Compounds	
Flavanones	Demonstrates both anti-oxidant and anticancer activity Flavones Possess antioxidant activity and effective against cancer. Flavanols Antioxidant activity
Curcumin	Strongly anti-inflammatory and strongly antioxidant, effective anti-clotting agent[52]
Glucosinolates	Anticancer activity, protect against bladder cancer[53]
Phytoestrogens	
Isoflavones	It Lowers LDL cholesterol, antioxidants, protects against prostate, breast, bowel and other cancers[54]
Lignans	Protect against development of cancer like colon and breast cancer[55]
Fatty Acids	
Omega 3 fatty acids	They are the Potent controllers of the inflammatory processes, help in Maintenance of brain function[56]&Reduce cholesterol disposition.
Fatty acids	Lower down the chances of coronary heart disease[57]
Prebiotics/Probiotics	They help to Improve Gastro Intestinalhealth[58]

Minerals	They are the important constituents of balanced diet
Polyols sugar alcohols (xylitol, sorbitol)	They may reduce the risk of dental cavities[59]

Table 4: Commercially available Nutraceuticals[60]

S.No	Product	Category	Benefit	Manufacturer
1	Glucon D	Glucose	Energy provider	Heinz
2	Proteinex	Protein and nutritional supplement	mental growth	Pfizer
3	GRD	Nutritional supplement	Tissue growth and repair	Zydus
4	Tropicana	Energy drink	Full of nutrients	Tropicana Products
5	B-Protein	Nutritional supplement	Formation of haemoglobin	British Biologicals
6	Cod liver Oil	Omega 3 fatty acids	Immunity booster	Sanofi
7	Revital	Health supplement	Improve health and immunity	Ranbaxy
		Nutritional supplement	Helps in child growth	Abott
9	Threptin diskette	Protein supplement	Ensures protein nutrition in body	Raptakos Brett &

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Topical Antimicrobial Polyherbal Formulation: Preparation and Evaluation of Different Parameters

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ABSTRACT:

Today utilization of herbal medicines have been increasing rapidly. Herbal medicines in skin related disorders are gaining more acceptance with the belief that they're safer with fewer side effects than others. The main objective of present work was to formulate and evaluate the polyherbal ointment containing leaves extract of Neem (*Azadirachtaindica*) and Tulsi (*Ocimum tenuiflorum*) with antimicrobial activity. The hydroalcoholic extracts were prepared by using cold maceration method. The different ointment bases were prepared. After completion of formulation they were evaluated for its physicochemical parameters like nature, colour, odour, pH, spreadability, extrudability, consistency, skin irritation and gave satisfactory results. The best formulation was used for antimicrobial activity against *Staphylococcus aureus.* Antimicrobial activity of the prepared formulation was compared with a marketed formulation (10 % w/w Betadine). Overall result of this study reveals that this is an effective polyherbal antiseptic ointment.
Keywords: Herbal Medicine, Neem, Tulsi, polyherbal, Antimicrobial.

INTRODUCTION

Medicinal plants have been known for their multiple disease curing properties from thousands of years and number of drugs have been isolated from natural sources, based on their use in the traditional medicine.[1] Natural phytochemicals isolated from fruits, vegetables and herbs possess a wide range of pharmacological effects, including antioxidant, antimicrobial and anti-inflammatory actions etc.[2] There are many reasons for the increased acceptance of the herbal medicines like products obtained from 'nature' and 'safer' than conventional medicine.[3] Pharmaceutical semisolid preparations include ointments, pastes, cream, emulsions, gels, and rigid foams.[4] The common property of semisolid is the ability to remain at the surface of application for reasonable duration before they are washed or worn off.[5] This adhesion property of semisolid is due to their plastic and rheological behavior, which allows the semisolids to retain their shape and adhere as a film until acted upon by an external force. After applying the force they deform and flow. [4] A typical human skin has three layers. Beneath the surface of the skin are nerves, nerve ending, glands, hair follicles and blood vessels.[6] When we add two or more herbs in the formulation they are known as Polyherbal formulations.[7,8] Polyherbal Antibacterial activity is the ability of the substance to inhibit or kill bacterial cells. Microorganisms like *Staphylococcus aureus* and *Escherichia coli* are the main pathogen that can cause many types of skin-related diseases such as skin rashes, acne, eczema, psoriasis, dermatitis etc.[9] Topical ointment containing extract of medicinal plant is one alternative to treat the skin infection caused by bacteria and prevent the use of oral antibiotic which then can develop bacterial-resistant.[10] Present research work was aimed at formulation and evaluation of Polyherbal semisolid dosage forms containing leaves extracts of *Azadirachta indica and Ocimum tenuiflorum.*

MATERIAL AND METHODS: Collection of plant material:

The plants *(Azadirachta indica and Ocimum tenuiflorum)* were collected from the herbal garden of Sunder Deep Pharmacy College

Extraction process

The collected plants *(Azadirachta indica & Ocimum tenuiflorum)* were extracted by cold maceration process. 100g of dried and powdered leaves of the plants were kept in contact with hydro alcoholic mixture (alcohol: distilled water in the ration of 1:3). The extraction was carried out for 3 days. After extraction, the solvents were evaporated and the concentrated residue was obtained.

Powdered *Tulsi* Leave

Powdered Neem Leaves

Formulation of Ointment: Required quantities of emulsifying wax, liquid paraffin and white soft paraffin were weighed and melted. To this, adequate quantities of hydro alcoholic extract of the mentioned two plants were added and stirred well until a homogeneous mass were obtained. This was termed as formulation F1. Similarly the ointments were prepared by the fusion method for the Absorption base (Formulation F2) and Hydrocarbon base (Formulation F3).

Table.1 Composition of Ointment Bases

S.No	Ingredients	Emulsifying Base (F1)	Absorption Base (F2)	Hydrocarbon Base (F3)
1.	Yellow Soft Paraffin	-	-	-
2.	Wool Alcohol	-	-	-
3.	White Petrolatum	5	8.5	9
4.	Hard Paraffin	-	0.5	0.3
5.	White Beeswax	-	-	0.2
6.	Liquid Paraffin	2	-	-
7.	Cetostearyl Alcohol	-	0.5	0.5
8.	Wool Fat	-	0.5	-
9.	Emulsifying Wax	3	-	-
10.	Purified Water	q.s. to 10 g	q.s. to 10 g	q.s. to 10 g

Table.2 Formula for Herbal Ointment

INGREDIENTS	QUANTITY TAKEN
Neem Extract	0.2 g
Tulsi Extract	0.2 g
Ointment Base	q.s. to 10 g

EVALUATION OF OINTMENT FORMULATION:

a. Color and Odour: - Colour and odour was examined by visual examination.

b. pH: The pH of the prepared formulation was determined by using Digital pH meter. One gram of ointment was dissolved in 100 ml of distilled water and stored for two hours.

c. Spreadability Test: Spreadability is a term expressed to denote the extent of area to which the ointments readily spreads on application to skin or affected part. The spreadability was expressed in terms of times in seconds taken by two slides to slip off from ointment and placed in between the slides under the direction of certain load. Lesser the time taken for separation of two slides, result the better spreadability. Spread ability was calculated by using the formula.

$S = (M.L/T)$ Where,

S = Spreadability,

M = Weight tied to upper slide,

L = Length of glass slides and

T = Time taken to separate the slides

d. Extrudability: A simple method was adopted for this study. The formulations were filled in the collapsible tubes afterthe ointments were set in the container. The extrudability of the different ointment formulations was determined in terms of weight in grams required to extrude a 0.5 cm of ribbon of ointment in 10 second.

e. Viscosity: Viscosity of ointment was measured by using Brookfield viscometer with spindle # 7.

f. Stability Study: A physical stability test of herbal ointment was carried out at 80°C for 50°C and stability was carried out for one month. The different parameter such as color, odor, texture, traces of gritty particles, skin irritation test were studied for all formulation in the first month.

g. Antimicrobial activity: In-vitro antimicrobial screening was performed by *Cylinder Plate Method.* The antimicrobial activity was performed on the ointment prepared using hydroalcoholic extract of the leaves of *Azadirachta indica, and Ocimum tenuiflorum.* Activity was performed against the pathogenic bacteria *Staphylococcus aureus.* A hole was bored at the centre of the solidified nutrient agar media inoculated with microorganisms and standard and test sample was placed in it. They are then incubated for about 18 hours at 37°C. After incubation, the zone of inhibition was noted.

OBSERVATION AND RESULTS Evaluation of Ointment

Table.3 Physicochemical Evaluation Parameters for Ointments

Table 4.2 Evaluation of antimicrobial activity by Cylinder Plate Method

Preparation	Zone of Inhibition
4% Polyherbal ointment (Absorption Base)	0.2 cm
10% betadine ointment	0.35 cm

Literatures revealed that herbs *Azadirachta indica, Ocimum tenuiflorum* have antibacterial activity. Hence an attempt was made to formulate a 4% polyherbal ointment and to evaluate for its physical parameter and antimicrobial activity by Cylinder Plate Method. Further the prepared formulation was compared for its antibacterial activity with a marketed formulation (10% w/w Betadine).Extract was prepared using cold maceration process. Cold Maceration process was adopted to prevent loss of active constituents. Hydroalcoholic solvent was used for extraction. In the present study, polyherbal ointments were prepared by fusion method using absorption base, emulsifying base and hydrocarbon base. The formulations were then evaluated for their physical parameters and compared with marketed 10%w/w Betadine ointment for its antibacterial activity. These physical parameters were within the acceptable range. The antibacterial activity of prepared ointments was compared with10%w/w Betadine ointment using *Staphylococcus aureus* (24 hours old culture). Antimicrobial studyshows that the prepared ointments have good activity against *Staphylococcus aureus*. Its activity is comparable to standard 10% Betadine ointment. Hence the study concludes that an efficient antiseptic ointment with antimicrobial activity can be formulated from the hydroalcoholic plant extracts of *Azadirachtaindica and Ocimumtenuiflorumwhich* can also be used for treating various types of skin infections.

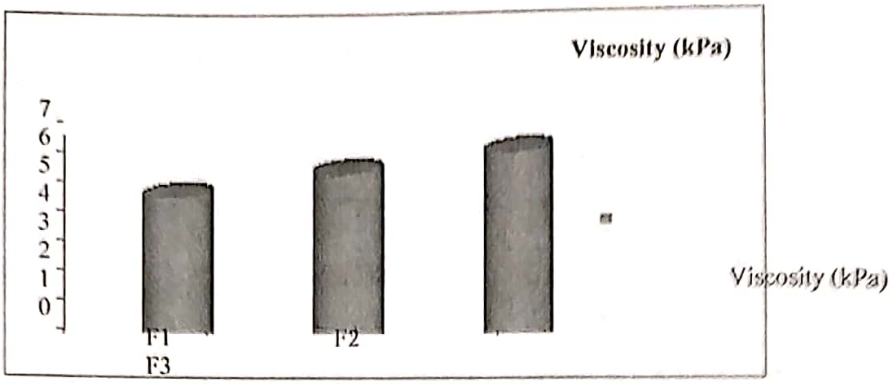

Figure-1: Viscosity of Formulation F1, F2 and F3

Spreadability (g.cm/min)

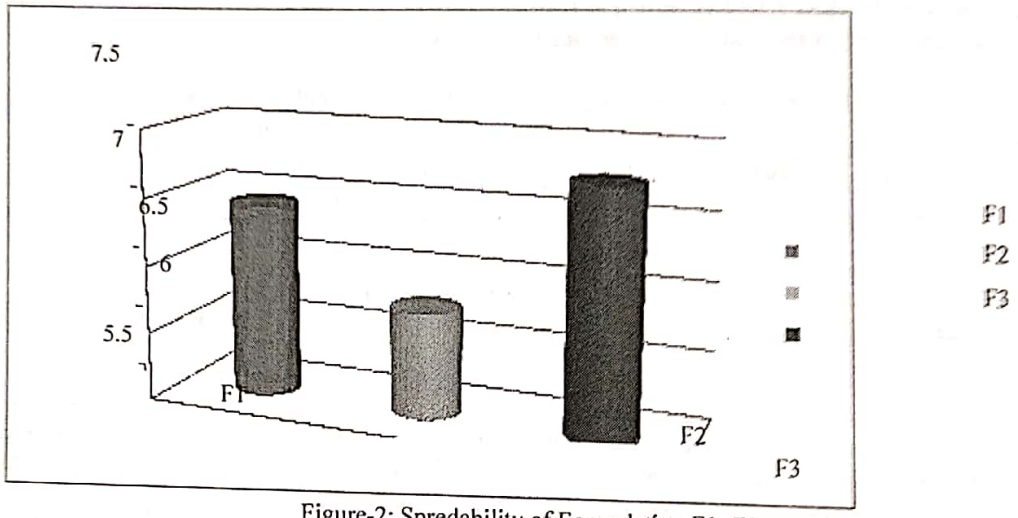

Figure-2: Spredability of Formulation F1, F2 and F3

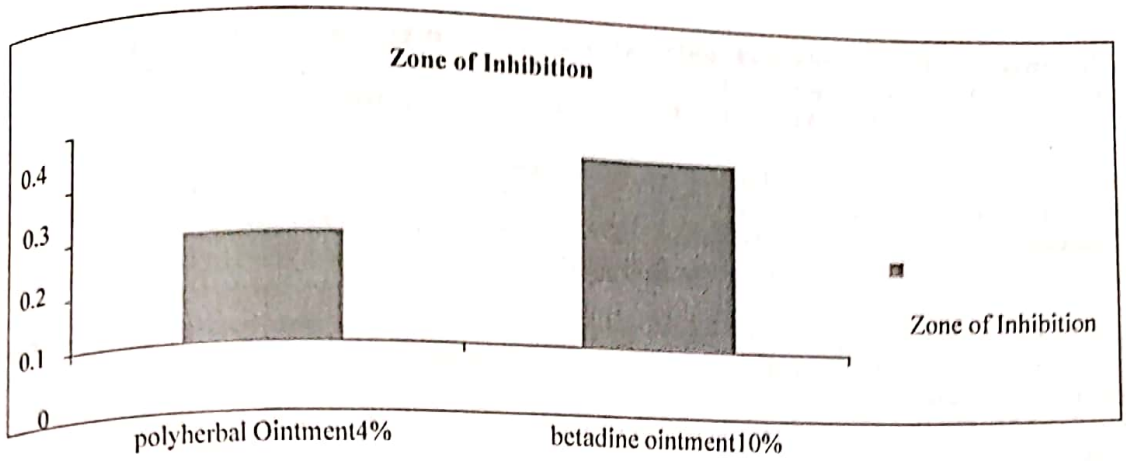

Figure-3: Zone of Inhibition (in cm)

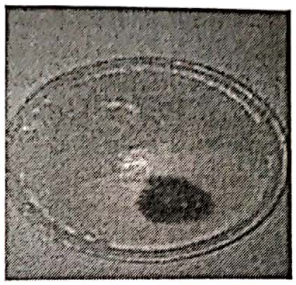

Figure-4: Zone of Inhibition

CONCLUSION

The purpose of the study was to prepare antimicrobial polyherbal ointment using locally available plants. On the basis of antimicrobial efficacy, two different local plants were taken and their hydro alcoholic extracts were incorporated in the most effective ratio in appropriate base. The final product readily spread on skin surface, showed no irritant effect, diffused well and was stable at different temperatures and having effective antimicrobial activity.

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