APPENDIX


Current Understanding of Synthesis and Pharmacological Aspects of Silver Nanoparticles

Shyam Baboo Prasad¹, Vidhu Aeri¹, Vashwan¹

¹School of Pharmaceutical Sciences, Lovely Professional University, Phagwara (Punjab)
²Faculty of Pharmacy, Jamia Hamdard, Hamdard Nagar, New Delhi

ABSTRACT

Silver nanoparticles (SNPs) are one of the most frequently used nanomaterials because of their antimicrobial properties. It can be prepared by physicochemical and biological methods. Silver ions have toxic effects on many pathogens, including bacteria, viruses, and fungi. Because of their low toxicity and size, it has been used in various medical applications. Decrease in particle size of silver nanoparticles may lead to an increase in antibacterial activity which has been associated with the increasing surface area to mass ratio. As various diseases are triggered by these microorganisms, so pharmacological evaluation of silver nanoparticles may be fruitful in those diseases which occur due to bacteria, fungi and virus. The present review deals with various method of preparation and reported preclinical activity of silver and its derivatives.

Keywords: Silver nanoparticles, Nano crystalline silver, Nanomedicine, Metallic nanoparticles, Silver.

INTRODUCTION

Nanotechnology is emerged as a fastest growing field with numerous applications in science and technology for manufacturing new materials. Nanotechnology is defined as the design, characterization and application of structures, devices and systems by controlling shape and size at 1 to 100 nm. Modern era is of nanomedicine owing to their various therapeutic applications with more efficacies and lesser side effects. The popularity is due to their potential for achieving specific process and selectivity in pharmacological action. Metallic nanoparticles, including gold, silver, iron, zinc and metal oxide nanoparticles, have shown great promise in biomedical application, due to their large surface area to volume ratio. SNPs or nanosilver (NS) are emerging as one of the fastest growing product in nanotechnology industry. In daily life NS is used in room spray, wall paints, water purifier and laundry detergent. SNPs are also incorporated in textiles for manufacturing of cloth, vests, underwear and socks. It is estimated that all nano...
DEVELOPMENT OF QUALITY STANDARDS OF ANCIENT SILVER BASED NANOMEDICINE: RAUPYA (SILVER) BHASMA

Shyam Baboo Prasad¹, Yashvanti¹, Madhurima Bhargava¹, Vidhu Aeri¹
¹School of Pharmaceutical Sciences, Lovely Professional University, Punjab (India)
²Department of Rashtraswar, Dayanand Ayurvedic College, Punjab (India)
³Faculty of Pharmacy, Jamia Hamdard, New Delhi (India).

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ABSTRACT

Health practitioners afraid to use metal as medicine due to reported severe toxicity. However Ayurvedic system of medicine particularly Rashashanta described about metal based medicine to cure various ailments. From ancient times bhasma is used in various diseases and found to be free from toxicity. As per Ayurvedic physician bhasma may be toxic if it is not prepared as per standard method mention in Rashashanta. Raupya bhasma is silver based nanomedicine of ancient Ayurveda which is used to strengthening brain, liver, heart and memory. It is also used as immunosuppressor and aphrodisiac. Due to lack of scientific data over Raupya bhasma it is not as popular as other silver nanomedicine. To consider above mention fact an attempt has been taken to prepare Raupya bhasma according to ancient literature and characterisation by modern analytical techniques. In this work, we present a systematic characterization of this traditional drug using various techniques like inductive coupled plasma mass spectroscopy (ICP-MS), X-ray diffraction (XRD), thermo gravimetric analysis (TGA), scanning electron microscopy (SEM), Fourier transform infrared spectroscopy (FTIR) and zeta size. The silver content in bhasma was found to be 63.05±4%. The nature of bhasma was found to be microcrystalline irregular having particle size 3.53±8 nm. TGA analysis indicates about loss of weight with temperature. The results obtained were found to satisfactory and confirm the traditional evaluation process by modern method. In addition, some specific findings were also made which could be used as standard data for quality control of Raupya bhasma.

Corresponding author

Dr. Vidhu Aeri
vidhuai@yahoo.com
Associate Professor
Department of Pharmacognosy and Phytochemistry
Faculty of Pharmacy, Jamia Hamdard, New Delhi-110062

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Formulation and Evaluation of Dosage form of Raupya (Silver) bhasma for colon targeted drug delivery

Shyam Baboo Prasad¹, Yashwant¹, Vidhu Aeri²*

¹. School of Pharmaceutical Sciences, Lovely Professional University, Phagwara (Punjab).
². Faculty of Pharmacy, Jamia Hamdard, Hamdard Nagar, (New Delhi).

ABSTRACT

The potential of guar gum as a film coating material for colon targeted delivery of raupyabhasma is assessed in this study. The granules was prepared by mixing raupyabhasma, guar gum and xanthan gum which was coated by guar gum and pH-sensitive polymer eudragit FS30D sequentially around drug-loaded granules. The outer eudragit FS30D coating defends the system against gastrointestinal environment and dissolves rapidly in distal small intestine, where a lumen pH of over 7 triggers the dissolution of the enteric polymer. The inner guar gum coating works as a time-controlled retardant and offers additional protection of the granules until it is degraded by microbes at the proximal colon. In vitro results indicate that guar gum followed by eudragit FS30D coating is a feasible coating material to achieve colon specific drug delivery.

Keywords: Colon targeting, Microbially triggered drug delivery to colon, Polysaccharide based drug delivery, Colon targeted drug delivery, Silver nanoparticles, Bhasma etc.

*Corresponding Author Email: vidhuseri@yahoo.com
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In vitro anti-inflammatory activity of Raupya (Silver) Bhasma

Shyam Babun Prasad1, Yashwantrao and Vidhu Arri2

1School of Pharmaceutical Sciences, Lovely Professional University, Phagwara (Punjab)
2Faculty of Pharmacy, Jamia Hamdard, New Delhi

ABSTRACT

Formulation of silver nitrate and silver sulfadiazine is choice of drug in topical treatment of burns and related inflammation. Ancient silver based nanomedicine of Ayurveda is Raupya bhasma (RB) used in treatment of different ailments but RB is still explored in their anti-inflammatory activity. To consider this an attempt has been made to evaluate in-vitro anti-inflammatory activity of RB against denaturation of protein. Denaturation of tissue proteins is one of the well-documented causes of inflammation. Different concentration of RB was incubated with egg albumin in specified experimental conditions and subjected to determination of absorbance and viscosity to assess the in-vitro anti-inflammatory property using diclofenac sodium as standard against denaturation of protein. RB inhibited protein denaturation in dose dependent manner. The effect of RB as anti-inflammatory agent was found to be better than standard (diclofenac sodium) at the IC50 value of RB and diclofenac sodium are 41.2 μg/mL and 46.1 μg/mL respectively. Inhibition of denaturation of protein was further confirmed by change in viscosity. On the basis of present research it is concluded that RB possessed marked anti-inflammatory activity against the denaturation of protein.

Keywords: Raupya bhasma, Silver nanoparticle, Anti-inflammatory activity, In vitro anti-inflammatory activity, Inflammation.

INTRODUCTION

Inflammation is a process of body defence mechanism, which is associated with pain and involves the increase in vascular permeability, increase of protein denaturation and membrane alteration. Inflammation may be due to chemical agents, physical agents and microbes. It is characterized by swelling, redness, pain, heat and loss of function of injured area[1]. Injury of cells may leads to release of kinins, prostanoids and histamine. The release of these mediators causes vasodilation, increase in permeability of the capillaries which may leads to increased blood flow to injured site. Inflammation can be classified as both acute an chronic. Acute inflammation is the initial response of the body to harmful stimuli and is achieved by the increased movement of plasma and leukocytes (especially granulocytes) from the blood into the injured tissues [2]. A cascade of biochemical events propagates and matures the inflammatory response, involving the local vascular system, the immune system, and various cells within the injured tissue. Prolonged inflammation is known as chronic inflammation, leads to a progressive shift in the type of cells present at the site of inflammation and is characterized by simultaneous destruction and healing of the tissue from the inflammatory process. Current drugs available for treatment of inflammation such as opioids and non-steroidal anti-inflammatory drugs (NSAIDs) are not useful in all cases of inflammatory disorders, because of their severe side effects. As a result, a search for other alternatives seems necessary and beneficial[1,2,3]. From the history of civilization traditional medicines were used to cure human ailments in every possible condition. In modern era we have the option to use them over the synthetic molecules because traditional drugs have fewer side effects[4]. Modern era is of nanomedicine owing to their various therapeutic applications with more efficacy and lesser side effects. The popularity is due to their potential for achieving specific process and selectivity in pharmacological action[5]. Bhasma the ancient concept of nanomedicine is used for treatment of various chronic diseases due to their unique properties.
Bhasma: Traditional Concept of Nanomedicine and Their Modern Era Prospective

Shyam Baboo Prasad¹, Yashwanth³, *Vidhu Aeri²

¹School of Pharmaceutical Sciences, Lovely Professional University, Phagwara (Punjab)  
²Faculty of Pharmacy, Jamia Hamdard, New Delhi-110062.

ABSTRACT

Bhasma is used as medicine from ancient time for treatment of various diseases. But health professional afraid to use metal product as medicine. As per Ayurvedic alchemists bhasma is safe to use only when it is prepared as per protocol mention in Rasashastra. The quality of bhasma can be assured by ancient Ayurvedic literature but it is not accepted in modern society. To trigger the research in field of bhasma present review deals with general method of preparation, characterisation and reported preclinical activity of bhasma.

Key words: Bhasma, Nanomedicine, Nanoparticle, Metallic nanoparticles, Herborineral, Ayurveda

INTRODUCTION

Nanomedicine is getting popularity day by day owing to their various therapeutic applications with more efficacies and lesser side effects. The popularity is due to their specific and selective pharmacological action. Bhasma, the ancient concept of nano medicine is used treatment of various chronic ailments since 7th century BC. From the history of civilization traditional medicines were used to cure human ailments in every possible condition. In modern era we have the option to use them over the synthetic molecules because they have lesser side effects. Bhasma is the calcination product of inorganic and organic substances. Bhasma as a medicine is a mystery due to severe side effect associated with metal when administered internally. As per Ayurvedic physician bhasma is nontoxic if metal is processed according to ancient Ayurvedic literature. The rational pharmacological and therapeutically approach of Ayurveda in general and Rasa shashtra in particular has transformed metal into medicinal form. The processes of shodhana (purification/potentiation) and marana (calcination/detoxification – treatment with that quantum of energy which is needed for physico-chemical conversion of raw materials to Bhasma: a therapeutic form) which are very individualized in terms of material, media, method and absolute medicinal form. The bhasmas are taken along with milk, butter, honey, or ghee which makes these elements easily assimilable, eliminating their harmful effects and enhancing their biocompatibility. Our ancient literature describes various methods to ensure the quality of bhasma. In current few year tremendous work has been carried out to ensure the quality of bhasma. The present review deals with ancient as well as modern method of preparation of bhasma, therapeutic application of almost all bhasma and their method of characterisation by traditional method (as per ancient literature) and using modern analytical techniques. Preparation of Bhasma: Bhasma can be prepared by purpaka method and kuspakka method. Summarised method of preparation is shown in figure-1. In recent time burning (Calcination) process is done in crucible at specific temperature as per nature of metal and the remaining procedure is kept same for preparation of bhasma. Bhasma as nano medicine: Bhasma is considered as biologically produced nanomedicine as the size of individual particle is found in nanorange. Heating of metal during shodhana may leads to increase in tension causing expansion of metal foil followed by cooling in liquid media leads to decrease in tension and increase in compression force. Repeated heating and cooling process may leads to brittleness, reduction in hardness and finally reduction in particle size. It is confirmed by various research carried out for characterisation of bhasma. The size of swarna bhasma and silver bhasma were found to be of 56 and 16 nm respectively. Chemical nature of bhasma: Bhasma is produced by the process of calcination of metal and minerals. Calcination of metal may leads to conversion of metal into its metallic oxide. Major chemical composition of bhasma is reported in table-1. Evaluation of bhasma: The quality of bhasma can be evaluated by traditional method of evaluation (Bhasma pariksha). Evaluation can be done by physical and chemical test. Physical test: Bhasma can be observed under bright sunlight to detect the presence and absence of lustre. A good quality of bhasma should be free from metallic lustre indicating metal is completely converted in to ash.

*Author for correspondence: E-mail: vidhuacer@yahoo.com
Appendix

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Review Article

Approaches for Targeted Drug Delivery to Colon

Shyam Baboo Prasad1, Vidhu Aeri2, *Yashwan1

1School of Pharmaceutical Sciences, Lovely Professional University, Phagwara (Punjab).
2Faculty of Pharmacy, Jamia Hamdard, Hamdard Nagar, (New Delhi).

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ABSTRACT
The conventional drug delivery system for colonic disease may lead to absorption of drug across biological membrane of gastrointestinal tract (GIT). The absorption of drug throughout GIT may lead to increase in dose and associated side effects. Colon targeted drug delivery (CTDD) is a method of delivering medication to a patient in a manner that increases concentration of the medication in colon relative to other part of GIT. The aim of CTDD is to prolong, localize, target and have protected drug interaction to diseased tissue. The present review deals with primary as well as recent approaches of delivery of drug to colon.

Key words: Colon targeting, Colon targeted drug delivery, Targeted drug delivery, Drug delivery, colon.

INTRODUCTION
The aim of targeted drug delivery (TDD) is selective and effective localization of drug into the target at therapeutic concentrations with limited or no access to non-target sites. A targeted drug delivery system is chosen in drugs having instability, low solubility, short half-life, large volume of distribution, poor absorption, low specificity and low therapeutic index1,2. TDD may provide maximum therapeutic activity by preventing degradation or inactivation of drug during transit to the target site. It can also minimize adverse effects because of inappropriate disposition and minimize toxicity of potent drugs by reducing dose. The colon is a site where local and systemic delivery of drugs can take place. Local delivery allows topical treatment variety of bowel diseases such as ulcerative colitis, Crohn’s disease, anastomosis, colon cancer and local treatment of colonic pathologies.3, 5, 6. The colon specific drug delivery system (CTDS) can be used for systemic delivery of protein and peptide drugs. However, treatment can be made effective if the drugs can be targeted directly into the colon, thereby reducing the systemic side effects.

Primary Approaches for Colon targeted drug delivery: Primary approaches that are used for colon targeted drug delivery (CTDDs) are as follow:

pH Sensitive Polymer Coated Drug Delivery: The pH Sensitive polymer coated drug delivery to colon can be achieved as the pH along the gastrointestinal tract (GIT) varies as shown in table 1. This can be accomplished by means of coating that are intact at lower pH of the stomach that will dissolved at neutral pH of the colon. These polymers used for coating should be resistant to the acidic condition of the stomach but ionize and get dissolved above a certain threshold alkaline pH found in small intestine. Thus, it is possible to apply same concept to deliver drugs to the terminal ileum or colon by use of enteric polymers with a relatively high threshold pH for dissolution and subsequent drug release. The most frequently used polymer for this purpose is methacrylic acid and methylmethacrylate that dissolve at pH 6 (Eudragit L) and pH 7 (Eudragit S) have been investigated. But the pH of the distal is 6. This delivery system thus has a inclination to release the drug load prior to reaching the colon. To overcome the problem of premature drug release, a copolymer of methacrylic acid, methyl methacrylate and ethyl acrylate (Eudragit FS) which dissolve at slower rate and at higher threshold pH 7 to 7.5 was reported. One must question the impact of gastrointestinal disease on targeting performance since patient with ulcerative colitis are known to have markedly low colon pH.7-9. Polymer used in pH Sensitive Polymer Coated Drug Delivery is shown in Tab1.

Time dependent drug delivery: In this approach, drug release to colon from the system after a predetermined lag time. The normal transit time in the stomach is 2 hr which may vary, while in the small intestine it is relatively constant around 3 hr. For the colon targeted drug release, the lag time should similar to the time taken for the system to reach the colon. The lag time of 3 hr is considered sufficient on the basis of relatively constant transit time in the small intestine (3hr). The lag time (lag time upon the gastric motility and size of the dosage form). One of the most primitive methods is the Pushnagap device. This device consists of a naso-disintegrating half capsule body sealed at the open end with a hydrogel plug, which is enclosed by a water-soluble cap. The whole unit is coated with an enteric polymer to avoid the difficult of variable gastric emptying. When the capsule pass in the small intestine, the enteric coating dissolves and the hydrogel plugs swells. The quantity of hydrogel is adjusted so that it peps out only after the specified period of time to release the contents. In another approach, organic acids are filled into the body of

*Author for correspondence: E-mail: yash99yash@gmail.com
Role of Traditional and Alternative Medicine in Treatment of Ulcerative Colitis

Shyam Baboo Prasad 1, Vidyut Aeri 2, *Yashwant 1

1School of Pharmaceutical Sciences, Lovely Professional University, Phagwara, Punjab, INDIA
2Faculty of Pharmacy, Jamia Hamdard, Hamdard Nagar, New Delhi, INDIA

Abstract
Currently available treatment options for ulcerative colitis (UC) in modern medicine have several adverse effects. Therefore, there is a need to develop safe and effective treatment modalities for ulcerative colitis (UC). Traditional and alternative medicine play an important role in the management of UC as they were developed from the experience of people which passed from one generation to next since history of civilization. This article presents a review on some reported traditional and alternative medicine for UC.

Key words: Ulcerative colitis, Inflammatory bowel disease, Colon, Inflammation, Traditional medicine, Herbal medicine etc.

Introduction
Inflammatory bowel disease (IBD) is a general term for a group of chronic inflammatory disorders of unknown etiology involving the gastrointestinal tract. Chronic IBD may be divided into two major groups, ulcerative colitis (UC) and Crohn’s disease (CD), clinically characterized by recurrent inflammatory involvement of intestinal segments with several manifestations often resulting in an unpredictable course 1. Ulcerative colitis is an inflammatory chronic disease primarily affecting the colorectal mucosa; the extent and severity of colon involvement are variable. In its most limited form it may be restricted to the distal rectum, while in its most extended form the entire colon is involved. However, 80% of the patients present with disease extending from the rectum to the splenic flexure, and only 20% have pancolitis 2. Although the causes of IBD remain unclear, considerable progress has been made recently in the identification of important pathophysiological mechanisms, and further research has been obtained from recent studies concerning their epidemiology, natural history, diagnosis, and treatment.

Symptoms
Initial symptoms of ulcerative colitis include diarrhea, blood in stool, pain, weight loss, arthritis, fever, loss of appetite, epistaxis, nausea, vomiting, abscesses, fistulas and lymph node swellings 2. Symptoms of mild, moderate, and chronic UC is reported in table 1.

Epidemiology
Ulcerative colitis is usually associated with recurrent attacks with complete remission of symptoms in the interim. The disease is more common in Caucasians than in blacks or Orientals with an increased incidence (three to sixfold) in Jews. Both sexes are equally affected. The peak occurrence of both diseases (UC and CD) is between ages 15 and 35, it has been reported in every decade of life. A familial incidence of IBD is currently recorded. In Asia, Africa and South America, cases of UC are reported less as compared to European country. Breast feeding, smoking and appendectomy are associated with reduced risk of UC. Depression, Western diet, left-handedness may increase risk of UC 3, 4.

Pathophysiology
The cause of UC still remains unclear, but on the basis of research in recent years point to an over stimulation or inadequate regulation of the mucosal immune system as a major pathophysiologic pathway, and particular emphasis has been given to either the study of mucosal inflammation or immunologic reactions. When the disease is active, the lamina propria of the mucosa becomes highly infiltrated with a mixture of acute and chronic inflammatory cells. There is a predominant increase in mucosal immunoglobulin (Ig) production, evidence of complement activation, and activation of macrophages and T cells. This immunological activity is associated with the release of a vast array of cytokines, kinins, leukotrienes, platelet activating factor (PAF) and reactive oxygen metabolites. These mediators not only serve to amplify the immune and inflammatory response, but they also have direct effects on epithelial function, on endothelial function (which may increase permeability and lead to ischemia), and on repair mechanisms, thus increasing collagen synthesis. In addition, many of the cytokines (interleukins 1 and 6, tumour necrosis factor) will activate an acute phase response, resulting in fever and a rise in serum acute phase proteins 3, 4.

Diagnosis
The diagnosis of UC is made on clinical suspicion and confirmed by biopsy, stool examinations, sigmoidoscopy or colonoscopy, or barium radiographic examination 4.

Complication

*Author for Correspondence: yash99yash@gmail.com
Probiotics: A Medieval To Modern Era Prospective

Shyam Baboo Prasad, Hitesh Verma, Vidhu Aeri, Yashwant

School of Pharmaceutical Sciences, Lovely Professional University, Phagwara (Punjab).
Faculty of Pharmacy, Jamia Hamdard, Hamdard Nagar, (New Delhi).

ABSTRACT
Probiotics have been perceived as a solution to many of the lifestyle related problems. In modern era the quality of water and food supply may affect the intestinal micro flora. Chlorinated water and preservatives added to foods may lead to an alteration in the normal micro biota of intestine. Probiotics, however, lead to reverses of this altered microbial picture back to normal. They tend to maintain the delicate balance existing between the gastro intestinal tract and the immunological system of the body. Whenever this balance is disturbed, a disease develops. Probiotics competitively inhibit the over stimulation of immune system by pathogenic bacteria by adhering themselves to the gastro intestinal mucosa in place of pathogenic bacteria and thus inhibiting their colonisation. They have proved to be beneficial in the case of allergies/eccema, diarrhoea, hyperlipidaemia, Acquired Immune Deficiency Syndrome, liver cirrhosis, gastric ulcer, hypertension, inflammation, arthritis, inflammatory bowel disease, peptic ulcers and cancer etc. It is also beneficial in case of antibiotic resistance or antibiotic associated side effects. The present review deals with the updated information about the role of probiotics in health and disease.

Key words: Probiotics, Lactobacillus, Bifidobacterium, Streptococcus, Saccharomyces, Healthcare

INTRODUCTION
Pharmacists have not been able to completely control the global morbidity and mortality in case of both acute and chronic diseases. Hence, search for the other alternatives has always been there. The old age quote of Hippocrates becomes most pertinent in the current health scenario i.e. “let food be thy medicine and medicine be thy food”1. In the late 90’s, microbiologists identified the difference between the micro flora of the diseased human beings and those of normal human beings. The beneficial micro flora were termed as “probiotics”2. There are billions of bacteria present in human Gastro Intestinal Track (GIT) forming about 1 kg of the human weight, which includes both harmful as well as beneficial bacteria. Together they are called as gut flora. Delicate balance between the harmful and the beneficial bacteria is responsible for maintenance of health. When this balance is disturbed, the person becomes diseased. One of the ways to regain this balance is the external administration of probiotics (beneficial bacteria) into the body of the diseased person. Probiotics include a large number of different types of bacteria that are normal inhabitants of human GIT. The most common among them are various species of Lactobacilli and Bifidobacteria. They reside in small intestine and colon. Probiotics have been able to attract the maximum attention among several food supplements as they have additional benefits beyond their nutritional value. In 1965, Stillwell and Lilly introduced the term “probiotics”3. The term is made up of two words Latin preposition pro means “for” and the Greek adjective bios (“life”). Hence, it means “for favour of life”. According to World Health organisation (WHO) and Food and Agriculture Organization (FAO) it is defined as “living microorganism intended for administration into the host body in adequate amount so as to confer health benefits”4. History: It has been known since long that there are benefits of using fermented milk products and prodiges of bread moulds. But Elie Metchnikoff started the probiotic therapy via fermented milk products in 1907. In 1915, the therapy was used for the treatment of urethral infections. However, in the intervening period of 70-80 decades less study is reported on probiotics due to an increased interest in antibiotics. These were labelled as “alternative medicines”. Recently there has been a resurgence of probiotics due to demand of consumers for better treatment. This resurgence can also be attributed to development of resistance against antibiotics. These were labelled as “alternative medicines”. Recently there has been a resurgence of probiotics due to demand of consumers for better treatment. This resurgence can also be attributed to development of resistance against antibiotics. These were labelled as “alternative medicines”. Recently there has been a resurgence of probiotics due to demand of consumers for better treatment. This resurgence can also be attributed to development of resistance against antibiotics. These were labelled as “alternative medicines”. Recently there has been a resurgence of probiotics due to demand of consumers for better treatment. This resurgence can also be attributed to development of resistance against antibiotics. These were labelled as “alternative medicines”. Recently there has been a resurgence of probiotics due to demand of consumers for better treatment. This resurgence can also be attributed to development of resistance against antibiotics. These were labelled as “alternative medicines”. Recently there has been a resurgence of probiotics due to demand of consumers for better treatment. This resurgence can also be attributed to development of resistance against antibiotics. These were labelled as “alternative medicines”. Recently there has been a resurgence of probiotics due to demand of consumers for better treatment. This resurgence can also be attributed to development of resistance against antibiotics. These were labelled as “alternative medicines”. Recently there has been a resurgence of probiotics due to demand of consumers for better treatment. This resurgence can also be attributed to development of resistance against antibiotics. These were labelled as “alternative medicines”. Recently there has been a resurgence of probiotics due to demand of consumers for better treatment. This resurgence can also be attributed to development of resistance against antibiotics. These were labelled as “alternative medicines”. Recently there has been a resurgence of probiotics due to demand of consumers for better treatment. This resurgence can also be attributed to development of resistance against antibiotics. These were labelled as “alternative medicines”.

Probiotic criteria: An organism must fulfill the following criteria in order to be considered as probiotics: There should be high cell viability, and should be able to survive in low pH. Even if strain cannot colonize in gut, it should have the ability to persist. They should have the ability to adhere to the epithelium of GIT so as to overcome the flushing effect due to peristalsis. They should have the ability to interact or to send signals to the immune cells associated with GIT. They should be capable of being isolated from humans. They should have processing resistance. They should be non-pathogenic. They should have positive influence on local metabolic activities. A dose of five billion colony forming units are generally recommended for adequate health benefits. Probiotics should be Generally Recognized as Safe (GRAS). Probiotics preparations involve the use of both single as well as mixture of microorganisms.

*Author for correspondence: E-mail: yash9yash@gmail.com