An Assignment on ROLE OF MICROOGRANISM IN PHARMACEUTICAL INDUSTRY

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ROLE OF MICROOGRANISM IN PHARMACEUTICAL INDUSTRIY

INTRODUCTION

Microbiology is the study of microorganisms such as bacteria, protozoa, fungi and similar organisms that can't be seen with the naked eye. The need to study these minute organisms started when scientists discovered the association of microbes to specific diseases. The roles of microbiology on the advances in the healthcare industry, especially in pharmaceutical and medical industry have led to great discoveries, from vaccines to devices. The growth of cosmetic industries also paralleled microbiological innovations, which in fact, paved the way to the study of cosmetic microbiology.

By nature, cells fight microbes that enter our body and this is commonly exhibited by pus formation and inflammation of wounds. Macrophages play an important role in immune system because they are capable of ingesting microbes that enter our body through open wounds. However, microbes could adapt and mutate rapidly, which results to opportunistic infectious diseases, such as HIV. On the contrary, microbes can also help us in ways like the way the "good bacteria" lactobacillus functions in our digestive system.

Understanding the principles of microbiology and human cell mechanisms allows pharmacists to discover antimicrobial drugs that would prevent an escalating number of communicable diseases. Pharmacists and microbiologists work synergistically to ensure that drug therapies target the opportunistic microbes without harming its human host. Another important role in pharmaceuticals is the use of microbes for the medically important studies, such as Bacteriorhodopsin, a protein from the plasma membrane of Halobacterium salinarum.

ROLE OF MICROORGANISM FOR PHARMACEUTICAL PRODUCT

The important products that manufactured by microorganism in pharmaceutical industry is described below-

VACCINE

A vaccine is a biological preparation that improves immunity to a particular disease. A vaccine typically contains an agent that resembles a disease-causing microorganism, and is often made from weakened or killed forms of the microbe, its toxins or one of its surface proteins. The agent stimulates the body's immune system to recognize the agent as foreign, destroy it, and "remember" it, so that the immune system can more easily recognize and destroy any of these microorganisms that it later encounters.

There are several types of vaccines in use. These represent different strategies used to try to reduce risk of illness, while retaining the ability to induce a beneficial immune response.

Types of Vaccine

Killed

Some vaccines contain killed, but previously virulent, micro-organisms that have been destroyed with chemicals, heat, radioactivity or antibiotics. Examples are the influenza vaccine, cholera vaccine, bubonic plague vaccine, polio vaccine, hepatitis A vaccine, and rabies vaccine.

Attenuated

Some vaccines contain live, attenuated microorganisms. Many of these are live viruses that have been cultivated under conditions that disable their virulent properties, or which use closely related but less dangerous organisms to produce a broad immune response. Although most attenuated vaccines are viral, some are bacterial in nature. They typically provoke more durable immunological responses and are the preferred type for healthy adults. Examples include the viral diseases yellow fever, measles, rubella, and mumps and the bacterial disease typhoid. The live Mycobacterium tuberculosis vaccine developed by Calmette and Guérin is not made of a contagious strain, but contains a virulently modified strain called "BCG" used to elicit an immune response to the vaccine.

Toxoid

Toxoid vaccines are made from inactivated toxic compounds that cause illness rather than the micro-organism. Examples of toxoid-based vaccines include tetanus and diphtheria. Toxoid vaccines are known for their efficacy. Not all toxoids are for micro-organisms; for example, *Crotalus atrox* toxoid is used to vaccinate dogs against rattlesnake bites.

Subunit

Protein subunit – rather than introducing an inactivated or attenuated micro-organism to an immune system (which would constitute a "whole-agent" vaccine), a fragment of it can create an immune response. Examples include the subunit vaccine against Hepatitis B virus that is composed of only the surface proteins of the virus (previously extracted from the blood serum of chronically infected patients, but now produced by recombination of the viral genes into yeast), the virus-like particle (VLP) vaccine against human papillomavirus (HPV) that is composed of the viral major capsid protein, and the hemagglutinin and neuraminidase subunits of the influenza virus. Subunit vaccine is being used for plague immunization.

Conjugate

Conjugate – certain bacteria have polysaccharide outer coats that are poorly immunogenic. By linking these outer coats to proteins (e.g. toxins), the immune system can be led to recognize the polysaccharide as if it were a protein antigen. This approach is used in the *Haemophilus influenzae* type B vaccine.

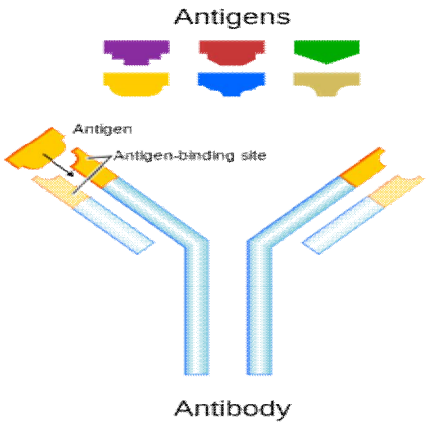
Valence

Vaccines may be *monovalent* (also called *univalent*) or *multivalent* (also called *polyvalent*). A monovalent vaccine is designed to immunize against a single antigen or single microorganism. A multivalent or polyvalent vaccine is designed to immunize against two or more strains of the same microorganism, or against two or more microorganisms. In certain cases a monovalent vaccine may be preferable for rapidly developing a strong immune response.

ANTIBODY

An antibody (Ab), also known as an immunoglobulin (Ig), is a large Y-shaped protein produced by B-cells that is used by the immune system to identify and neutralize foreign objects such as bacteria and viruses. The antibody recognizes a unique part of the foreign target, called an antigen. Each tip of the "Y" of an antibody contains a paratope (a structure analogous to a lock) that is specific for one particular epitope (similarly analogous to a key) on an antigen, allowing

these two structures to bind together with precision. Using this binding mechanism, an antibody can *tag* a microbe or an infected cell for attack by other parts of the immune system, or can neutralize its target directly (for example, by blocking a part of a microbe that is essential for its invasion and survival). The production of antibodies is the main function of the humoral immune system.



Antibodies are glycoproteins belonging to the immunoglobulin superfamily; the terms *antibody* and *immunoglobulin* are often used interchangeably. Antibodies are typically made of basic structural units—each with two large heavy chains and two small light chains. There are several different types of antibody heavy chains, and several different kinds of antibodies, which are grouped into different *isotypes* based on which heavy chain they possess. Five different antibody isotypes are known in mammals, which perform different roles, and help direct the appropriate immune response for each different type of foreign object they encounter.

ANTIBIOTICS

An antibacterial is an agent that inhibits bacterial growth or kills bacteria. The term is often used synonymously with the term *antibiotic(s)*. Today, however, with increased knowledge of the causative agents of various infectious diseases, *antibiotic(s)* has come to denote a broader range of antimicrobial compounds, including anti-fungal and other compounds.

The term *antibiotic* was first used in 1942 by Selman Waksman and his collaborators in journal articles to describe any substance produced by a microorganism that is antagonistic to the growth of other microorganisms in high dilution. This definition excluded substances that kill bacteria, but are not produced by microorganisms (such as gastric juices and hydrogen peroxide). It also excluded synthetic antibacterial compounds such as the sulfonamides. Many antibacterial compounds are relatively small molecules with a molecular weight of less than 2000 atomic mass units.

With advances in medicinal chemistry, most of today's antibacterials chemically are semisynthetic modifications of various natural compounds.[4] These include, for example, the beta-lactam antibacterials, which include the penicillins (produced by fungi in the genus *Penicillium*), the cephalosporins, and the carbapenems. Compounds that are still isolated from living organisms are the aminoglycosides, whereas other antibacterials for example, the sulfonamides, the quinolones, and the oxazolidinones—are produced solely by chemical synthesis. In accordance with this, many antibacterial compounds are classified on the basis of chemical/biosynthetic origin into natural, semisynthetic, and synthetic. Another classification system is based on biological activity; in this classification, antibacterials are divided into two broad groups according to their biological effect on microorganisms: bactericidal agents kill bacteria, and bacteriostatic agents slow down or stall bacterial growth.

PROBIOTICS

Probiotics are live bacteria that may confer a health benefit on the host. In the past, there were other definitions of probiotics. The first use of the word “Probiotic” as microorganisms that have effects on other microorganism was accredited to Lilly and Stilwell (1965), expressed as follows: Substances secreted by one microorganism that stimulate another microorganism. The probiotics are describing as “Organisms and substances that have a beneficial effect on the host animal by contributing to its intestinal microbial balance”. Later, the definition was greatly improved by Fuller in 1989, whose explanation was very close to the definition used today. Fuller in 1989 described probiotics as "live microbial feed supplement which beneficially affects the host animal by improving its intestinal microbial balance". He stressed two important facts of probiotics: the viable nature of probiotics and the capacity to help with intestinal balance. Alternative expert review indicates there is insufficient scientific evidence for supplemental probiotics having a benefit. Lactic acid bacteria (LAB) and bifidobacteria are the most common types of microbes

used as probiotics, but certain yeasts and bacilli may also be used. Probiotics are commonly consumed as part of fermented foods with specially added active live cultures, such as in yogurt, soy yogurt, or as dietary supplements. Probiotics are also delivered in fecal transplants, in which stool from a healthy donor is delivered like a suppository to an infected patient.

Table: Source of Probiotics and Effect on Body

Strain	Claimed potential effect in Body
Bacillus coagulans GBI-30, 6086	May improve abdominal pain and bloating in IBS patients. May increase immune response to a viral challenge.
Bifidobacterium animalis subsp. *lactis* BB-12	May have an effect on the gastrointestinal system.
Bifidobacterium longum subsp. *infantis* 35624	Possible relief from abdominal pain/discomfort, bloating and constipation.
Lactobacillus acidophilus NCFM	Shown in one study to reduce the side effects of antibiotic therapy.
Lactobacillus paracasei St11 (or NCC2461) *Lactobacillus johnsonii* La1 (= Lactobacillus LC1, *Lactobacillus johnsonii* NCC533)	May reduce incidence of *H. pylori*-caused gastritis and may reduce inflammation.
Lactobacillus plantarum 299v	May affect symptoms of IBS.
Lactobacillus reuteri ATCC 55730 (*Lactobacillus reuteri* SD2112)	Evidence for diarrhea mitigation in children, decreased crying in infantile colic, *H. pylori* infection, antibiotic-associated side-effects, fever and diarrhea in children and number of sick days in adults.
Lactobacillus reuteri Protectis (DSM 17938, daughter strain of ATCC 55730)	Evidence for shortened duration of diarrhea in children, decreased crying in infantile colic, reduced risk of diarrhea in children, may affect constipation and functional abdominal pain in children.
Lactobacillus reuteri Prodentis (DSM 17938/ATCC 55730 and ATCC PTA 5289 in combination) for oral health	Evidence for effect on gingivitis and periodontitis,[103][104][105][106] preliminary evidence for reduction of oral malodor, evidence for reduction of risk factors for caries.
Saccharomyces boulardii	Good evidence for treatment and prevention of antibiotic-associated diarrhea and acute diarrhea.
Tested as mixture: *Lactobacillus rhamnosus* GR-1 & *Lactobacillus reuteri* RC-14	In one study, oral ingestion resulted in vaginal colonisation and reduced vaginitis.
Tested as mixture: *Lactobacillus acidophilus* NCFM & *Bifidobacterium bifidum* BB-12	Preliminary evidence for reduced *C. difficile*–associated disease.

ENZYME PRODUCTION

There is a large number of microorganisms which produce a variety of enzymes. Enzymes differ with respect to substrates. Some of the microorganisms producing enzymes are listed in Table-

Microorganisms producing enzymes

Microorganisms		Enzymes
Bacteria	*Bacillus cereus*	Penicillinase
	B. coagulans	a-amylase
	B. licheniformis	a-amylase, protease
	B. megaterium	Penicillin acylase
	Citrobacter spp.	L-asparaginase
	Escherichia coli	Penicillin acylase, b-galactosidase
	Klebsiella pneumoniae	Pullulanase
Actinomycetes:	*Actinoplanes sp.*	Glucose isomerase
Fungi:	*Aspergilus flavus*	Urate oxidase
	A. niger	Amylases, protease, pectinase, glucose oxidase
	A. oryzae	Amylases, lipases, protease
	Aureobasidium pullulans	Esterase, invertase
	Candila lipolytica	Lipase
	Mucor micheli and M. pusillis	Bennet
	Neurospora crassa	Trysinase
	Penicillium funiculosum	Dextranase
	P. notatum	Glucose oxidase
	Rhizopus sp.	Lipase
	Saccharomyces cerevisiae	Invertase
	S. fragilis	Invertase
	Trichoderma reesei	Cellulase
	T. viride	Cellulase

VITAMIN PRODUCTION

Tab. 3. Microbial and Enzymatic Processes for the Production of Fat-Soluble Vitamins

Vitamin	Enzyme (Microorganism)	Method
Vitamin E and K_1 side chains	multiple enzyme system (*Geotrichum candidum*)	enzymatic conversion from (*E*)-3-(1′,3′-dioxolane-2′-yl)-2-butene-1-ol
[(*S*)-2-methyl-γ-butyrolactone]	reductase bakers' yeast, (*Geotrichum* sp., etc.)	asymmetric reduction of ethyl-4,4-dimethoxy-3-methylcrotonate
[(*S*)-3-methyl-γ-butyrolactone]	multiple enzyme system (*Candida* sp., etc.)	stereoselective oxidation of isobutyric acid
[(*S*)- or (*R*)-β-hydroxy-isobutyric acid]		
Vitamin K_2	multiple enzyme system (*Flavobacterium* sp.)	conversion of quinone- and side chain-precursors to the vitamin
Arachidonic acid	fermentation (*Mortierella alpina*)	fermentative production from glucose
Dihomo-γ-linolenic acid	fermentation (*Mortierella alpina*)	fermentative production from glucose by a Δ5-desaturase-defective mutant
Mead acid	fermentation (*Mortierella alpina*)	fermentative production from glucose by a Δ12-desaturase-defective mutant
Eicosapentaenoic acid	multiple enzyme system (*Mortierella alpina*)	Δ17-desaturation of arachidonic acid or conversion from α-linolenic acid

Tab. 2. Microbial and Enzymatic Processes for the Production of Water-Soluble Vitamins and Coenzymes

Vitamin, Coenzyme	Enzyme (Microorganism)	Method
Vitamin C (2-Keto-L-gulonic acid)	2,5-diketo-D-gulonic acid reductase (*Corynebacterium* sp.)	enzymatic conversion of 2,5-diketo-D-gluconate obtained through fermentative process to 2-keto-L-gulonic, followed by chemical conversion to L-ascorbic acid
Biotin	fermentation (*Serratia marcescens*)	fermentative production from glucose by a genetically engineered bacterium
	multiple enzyme system (*Bacillus sphaericus*)	conversion from diaminopimelic acid using the biotin biosynthesis enzyme system of a mutant of *B. sphaericus*
Pantothenic acid (D-Pantoic acid)	lactonohydrolase (*Fusarium oxysporum*)	resolution of D,L-pantolactone to D-pantoic acid and L-pantolactone by stereoselective hydrolysis
Coenzyme A	multiple enzyme system (*Brevibacterium ammoniagenes*)	conversion by enzymatic coupling of ATP-generating system and coenzyme A biosynthesis system of *B. ammoniagenes* (parent strain or mutant) with D-pantothenic acid, L-cysteine, and AMP (or adenosine, adenine, etc.) as substrates
Nicotinamide	nitrile hydratase (*Rhodococcus rhodochrous*)	hydration of 3-cyanopyridine
Nicotinic acid	nitrilase (*Rhodococcus rhodochrous*)	hydrolysis of 3-cyanopyridine to form corresponding acid (nicotinic acid) and ammonia

BACTERIOCINS

Bacteriocins are peptides that can be more readily engineered than small molecules, and are possible alternatives to conventional antibacterial compounds. Different classes of bacteriocins have different potential as therapeutic agents. Small-molecule bacteriocins (microcins and lantibiotics) are similar to the classic antibiotics; colicin-like bacteriocins possess a narrow spectrum, and require molecular diagnostics prior to therapy. Limitations of large-molecule antibacterials include reduced transport across membranes and within the human body. For this reason, they are usually applied topically or gastrointestinally.

CHELATION

Chelation of micronutrients that are essential for bacterial growth to restrict pathogen spread *in vivo* might supplement some antibacterials. For example, limiting the iron availability in the human body restricts bacterial proliferation. Many bacteria, however, possess mechanisms (such as siderophores) for scavenging iron within environmental niches in the human body, and experimental developments of iron chelators, therefore, aim to reduce iron availability specifically to bacterial pathogens.

ANTIMICROBIAL COPPER ALLOY SURFACES

Copper-alloy surfaces have natural intrinsic properties to effectively and quickly destroy bacteria. The United States Environmental Protection Agency has approved the registration of 355 different antibacterial copper alloys that kill *E. coli* O157:H7, *methicillin*-resistant *Staphylococcus aureus* (*MRSA*), *Staphylococcus, Enterobacter aerogenes,* and *Pseudomonas aeruginosa* in less than 2 hours of contact. As a public hygienic measure in addition to regular cleaning, antimicrobial copper alloys are being installed in healthcare facilities and in a subway transit system.

PHAGE THERAPY

Phage therapy is the use of viruses that infect bacteria (i.e. phages) for the treatment of bacterial infections. Phages are common in bacterial populations and control the growth of bacteria in many environments, including in the intestine, the ocean, and the soil. Phage therapy was in use in the 1920s and 1930s in the US, Western Europe, and Eastern Europe. However, success rates of this therapy have not been firmly established, because only a limited number of clinical trials testing the efficacy of phage therapy have been conducted. These studies were performed mainly in the former Soviet Union, at the Eliava Institute of Bacteriophage, Microbiology and Virology, Republic of Georgia. The development of antibacterial-resistant bacteria has sparked renewed interest in phage therapy in Western medicine. Several companies (e.g., Intralytix, Novolytics, and Gangagen), universities, and foundations across the world now focus on phage therapies. One concern with this therapeutic strategy is the use of genetically engineered viruses, which limits certain aspects of phage therapy.

ANTIMICROBIAL ACTIVITY AND DISINFECTION

Another major focus of pharmaceutical microbiology is to determine how a product will react in cases of contamination. For example: You have a bottle of cough medicine. Imagine you take the lid off, pour yourself a dose and forget to replace the lid. You come back to take your next dose and discover that you have indeed left the lid off for a few hours. What happens if a microorganism "fell in" whilst the lid was off? There are tests that look at that. The product is "challenged" with a known amount of specific microorganisms, such as E. coli and C. albicans and the anti-microbial activity monitored.

Pharmaceutical microbiology is additionally involved with the validation of disinfectants, either according to U.S. AOAC or European CEN standards, to evaluate the efficacy of disinfectants in suspension, on surfaces, and through field trials.

MEDICAL DEVICES

Microbiology plays a significant role in medical devices, such as fluorescent fusion, which are used for fast and precise detection of pathogens in tissue samples. It is a technology for carrying out immunofluorescence studies that may be applied to find specific cells in complex biological systems.

COSMETIC MICROBIOLOGY

According to International Microbiology, microbial contamination of cosmetic products is a matter of great importance to the industry and it can become a major cause of both product and economic losses. Moreover, the contamination of cosmetics can result in them being converted into products hazardous for consumers. The water and nutrients present in cosmetics make them susceptible to microbial growth, although only a few cases of human injury due to contaminated cosmetics have been reported. More often, microorganisms are the cause of organoleptic alterations, such as offensive odors, and changes in viscosity and color.

CONCLUSION

Industrial microbiology includes the use of microorganisms to manufacture food or industrial products in large quantities. Numerous microorganisms are used within industrial microbiology; these include naturally occurring organisms, laboratory selected mutants, or even genetically modified organisms (GMOs). Currently, the debate in the use of genetically modified organisms (GMOs) in food sources is gaining both momentums, with more and more supporters on both sides. However, the use of microorganisms at an industrial level is deeply rooted into today's society. The following is a brief overview of the various microorganisms that have industrial uses, and of the roles they play.

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