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Review Article

Identification of microbes: A Review

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Abstract

The present investigation deals with development of Hydroxypropyl methylcellulose (HPMC 15cps) based cephalexin extended release (ER) tablet by direct compression method, which can release the drug for six hours at predetermined rate. Different concentration of HPMC 15cps were taken from lower to higher concentration with respect to drug and study their effect on drug release and evaluate different formulation parameters like bulk density, tapped density, compressibility index, Hausner's ratio, tablet hardness, friability, uniformity of weight, uniformity of drug content and stability study. The result of extended release tablet formulation F-5 containing 13.3% HPMC 15cps with respect to drug shows drug release in six hours at predetermined rate from other 5 formulation. The dissolution results show that on a higher amount of HPMC 15cps in tablet composition resulted in reduced drug release. The tablets were prepared by direct compression method. Hardness was found to be in the range of 7.54±0.01to 10.24±0.03 kg/cm^2, the percent friability was in the range of 0.1022±0.02 to 0.3633±0.01 % and tablets showed 97.18±0.48 to 99.78±0.07% of the labeled amount of cephalexin indicating uniformity content. The effect of storage on *in vitro* release and physicochemical parameters of successful batch was studied and was found to be in acceptable limits.

Keywords: Cephalexin, Extended release tablet, Hydroxypropyl methylcellulose 15cps, *In vitro* dissolution

Introduction

An infectious disease is a clinically evident illness resulting from the presence of pathogenic biological agents, including pathogenic viruses, pathogenic bacteria, fungi, protozoa, multicellular parasites, and aberrant proteins known as prions. These pathogens are able to cause disease in animals and/or plants. Infectious pathologies are also called communicable diseases or transmissible diseases due to their potential of transmission from one person or species to another by a replicating agent (as opposed to a toxin).[1] Transmission of an infectious disease may occur through one or more of diverse pathways including physical contact with infected individuals. These infecting agents may also be transmitted through liquids, food, body fluids, contaminated objects, airborne inhalation, or through vector-borne spread.[2] Transmissible diseases which occur through contact with an ill person or their secretions, or objects touched by them, are especially infective, and are sometimes referred to as contagious diseases.

Infectious (communicable) diseases which usually require a more specialized route of infection, such as vector transmission, blood or needle transmission, or sexual transmission, are usually not regarded as contagious, and thus are not as amenable to medical quarantine of victims.

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The term *infectivity* describes the ability of an organism to enter, survive and multiply in the host, while the *infectiousness* of a disease indicates the comparative ease with which the disease is transmitted to other hosts.[3] An infection however, is not synonymous with an infectious disease, as an infection may not cause important clinical symptoms or impair host function.[2]

Classification:-

Among the almost infinite varieties of microorganisms, relatively few cause disease in otherwise healthy individuals.[4] Infectious disease results from the interplay between those few pathogens and the defenses of the hosts they infect. Primary pathogens cause disease as a result of their presence or activity within the normal, healthy host, and their intrinsic virulence (the severity of the disease they cause) is, in part, a necessary consequence of their need to reproduce and spread. Many of the most common primary pathogens of humans only infect humans, however many serious diseases are caused by organisms acquired from the environment or which infect non-human hosts. Organisms which cause an infectious disease in a host with depressed resistance are classified as *opportunistic pathogens*. Opportunistic disease may be caused by microbes that are ordinarily in contact with the host, such as pathogenic bacteria or fungi in the gastrointestinal or the upper respiratory tract. An opportunistic disease requires impairment of host defenses, which may occur as a result of genetic defects (such as Chronic granulomatous disease), exposure to antimicrobial drugs or immunosuppressive chemicals (as might occur following poisoning or cancer chemotherapy), exposure to ionizing radiation, or as a result of an infectious disease with immunosuppressive activity (such as with measles, malaria or HIV disease). Primary pathogens may also cause more severe disease in a host with depressed resistance than would normally occur in an immunosufficient host.[2] One way of proving that a given disease is "infectious", is to satisfy Koch's postulates (first proposed by Robert Koch), which demands that the infectious agent be identified only in patients and not in healthy controls, and that patients who contract the agent also develop the disease. These postulates were first used in the discovery that Mycobacteria species cause tuberculosis. Koch's postulates cannot be met ethically for many human diseases because they require experimental infection of a healthy individual with a pathogen produced as a pure culture. Often, even diseases that are quite clearly infectious do not meet the infectious criteria. For example, *Treponema pallidum*, the causative spirochete of syphilis, cannot be cultured *in vitro* - however the organism can be cultured in rabbit testes.

Transmission:- An infectious disease is transmitted from some source. Defining the means of transmission plays an important part in understanding the biology of an infectious agent, and in addressing the disease it causes.Transmission may occur through several different mechanisms. Respiratory diseases and meningitis are commonly acquired by contact with aerosolized droplets, spread by sneezing, coughing, talking, kissing or even singing. Gastrointestinal diseases are often acquired by ingesting contaminated food and water.

Sexually transmitted diseases are acquired through contact with bodily fluids, generally as a result of sexual activity. Some infectious agents may be spread as a result of contact with a contaminated, inanimate object (known as a fomite), such as a coin passed from one person to another, while other diseases penetrate the skin directly.[2] Biological vectors are often responsible for serious blood-borne diseases, such as malaria, viral encephalitis, Chagas disease, Lyme disease and African sleeping sickness. Biological vectors are usually, though not exclusively, arthropods, such as mosquitoes, ticks, fleas and lice. Vectors are often required in the life cycle of a pathogen. A common strategy used to control vector borne infectious diseases is to interrupt the life cycle of a pathogen by killing the vector. The relationship between virulence and transmission is complex, and has important consequences for the long term evolution of a pathogen. Since it takes many generations for a microbe and a new host species to co-evolve, an emerging pathogen may hit its earliest victims especially hard. It is usually in the first wave of a new disease that death rates are highest. If a disease is rapidly fatal, the host may die before the microbe can get passed along to another host.

History:- When the Black Death bubonic plague reached al-Andalus in the 14th century, Ibn Khatima and Ibn al-Khatib hypothesized that infectious diseases are caused by "contagious entities" which enter the human body.[25] Such ideas became more popular in Europe during the Renaissance, particularly through the writing of the Italian monk Girolamo Fracastoro.[26] Louis Pasteur proved beyond doubt that certain diseases are caused by infectious agents, and developed a vaccine for rabies. Robert Koch, provided the study of infectious diseases with a scientific basis known as Koch's postulates. Anton van Leeuwenhoek (1632–1723) advanced the science of microscopy by being the first to observe microorganisms, allowing for easy visualization of bacteria. Edward Jenner, Jonas Salk and Albert Sabin developed effective vaccines for smallpox and polio, which would later result in the eradication and near-eradication of these diseases, respectively.Alexander Fleming discovered the world's first antibiotic Penicillin which Florey and Chain then developed. Gerhard Domagk developed sulphonamides, the first broad spectrum synthetic antibacterial drugs.

Prevention:-One of the ways to prevent or slow down the transmission of infectious diseases is to recognize the different characteristics of various diseases.[5] Some critical disease characteristics that should be evaluated include virulence, distance traveled by victims, and level of contagiousness. The human strains of Ebola virus, for example, incapacitate its victims extremely quickly and kills them soon after.

Also, this virus must spread through skin lesions or permeable membranes such as the eye. Thus, the initial stage of Ebola is not very contagious since its victims experience only internal hemorrhaging. As a result of the above features, the spread of Ebola is very rapid and usually stays within a relatively confined geographical area. In contrast, Human Immunodeficiency Virus (HIV) kills its victims very slowly by attacking their immune system.[2] As a result, many of its victims transmit the virus to other individuals before even realizing that they are carrying the disease. Also, the relatively low virulence allows its victims to travel long distances, increasing the likelihood of an epidemic.

Another effective way to decrease the transmission rate of infectious diseases is to recognize the effects of small-world networks.[5] Another example is the use of ring culling or vaccination of potentially susceptible livestock in adjacent farms to prevent the spread of the foot-and-mouth virus in 2001.[7]

Immunity:- Infection with most pathogens does not result in death of the host and the offending organism is ultimately cleared after the symptoms of the disease have waned.[4] This process requires immune mechanisms to kill or inactivate the inoculum of the pathogen. Specific acquired immunity against infectious diseases may be mediated by antibodies.

- a direct effect upon a pathogen, such as antibody-initiated complement-dependent bacteriolysis, opsonoization, phagocytosis and killing, as occurs for some bacteria,
- neutralization of viruses so that these organisms cannot enter cells,
- by T lymphocytes which will kill a cell parasitized by a microorganism.

Resistance to infection (immunity) may be acquired following a disease, by asymptomatic carriage of the pathogen, by harboring an organism with a similar structure (crossreacting), or by vaccination. Knowledge of the protective antigens and specific acquired host immune factors is more complete for primary pathogens than for opportunistic pathogens. Some individuals develop natural serum antibodies to the surface polysaccharides of some agents although they have had little or no contact with the agent, these natural antibodies confer specific protection to adults and are passively transmitted to newborns.

Host genetic factors:- The clearance of the pathogens, either treatment-induced or spontaneous, can be influenced by the genetic variants carried by the individual patients. For instance, for genotype 1 hepatitis C treated with Pegylated interferon-alpha-2a or Pegylated interferon-alpha-2b (brand names Pegasys or PEG-Intron) combined with ribavirin, it has been shown that genetic polymorphisms near the human IL28B gene, encoding interferon lambda 3, are associated with significant differences in the treatment-induced clearance of the virus.

Diagnosis:- Diagnosis of infectious disease sometimes involves identifying an infectious agent either directly or indirectly. In practice most minor infectious diseases such as warts, cutaneous abscesses, respiratory system infections and diarrheal diseases are diagnosed by their clinical presentation. Conclusions about the cause of the disease are based upon the likelihood that a patient came in contact with a particular agent, the presence of a microbe in a community, and other epidemiological considerations. Given sufficient effort, all known infectious agents can be specifically identified. The benefits of identification, however, are often greatly outweighed by the cost, as often there is no specific treatment, the cause is obvious, or the outcome of an infection is benign. Specific identification of an infectious agent is usually only determined when such identification can aid in the treatment or prevention of the disease, or to advance knowledge of the course of an illness prior to the development of effective therapeutic or preventative measures. For example, in the early 1980s, prior to the appearance of AZT for the treatment of AIDS, the course of the disease was closely followed by monitoring the composition of patient blood samples, even though the outcome would not offer the patient any further treatment options. The development of molecular diagnostic tools have enabled physicians and researchers to monitor the efficacy of treatment with anti-retroviral drugs. Molecular diagnostics are now commonly used to identify HIV in healthy people long before the onset of illness and have been used to demonstrate the existence of people who are genetically resistant to HIV infection. Thus, while there still is no cure for AIDS, there is great therapeutic and predictive benefit to identifying the virus and monitoring the virus levels

within the blood of infected individuals, both for the patient and for the community at large. Diagnosis of infectious disease is nearly always initiated by medical history and physical examination. More detailed identification techniques involve the culture of infectious agents isolated from a patient. Culture allows identification of infectious organisms by examining their microscopic features, by detecting the presence of substances produced by pathogens.

Microscopy:- Another principal tool in the diagnosis of infectious disease is microscopy. Virtually all of the culture techniques discussed above rely, at some point, on microscopic examination for definitive identification of the infectious agent. Microscopy may be carried out with simple instruments, such as the compound light microscope, or with instruments as complex as an electron microscope. Samples obtained from patients may be viewed directly under the light microscope, and can often rapidly lead to identification. Microscopy is often also used in conjunction with biochemical staining techniques, and can be made exquisitely specific when used in combination with antibody based techniques. For example, the use of antibodies made artificially fluorescent (fluorescently labeled antibodies) can be directed to bind to and identify a specific antigens present on a pathogen. A fluorescence microscope is then used to detect fluorescently labeled antibodies bound to internalized antigens within clinical samples or cultured cells. This technique is especially useful in the diagnosis of viral diseases, where the light microscope is incapable of identifying a virus directly. The response of bacteria to different staining procedures is used in the taxonomic classification of microbes as well. Two methods, the Gram stain and the acid-fast stain, are the standard approaches used to classify bacteria and to diagnosis of disease. The Gram stain identifies the bacterial groups Firmicutes and Actinobacteria, both of which contain many significant human pathogens. The acid-fast staining procedure identifies the Actinobacterial genera *Mycobacterium* and *Nocardia*.

Biochemical tests:-- Biochemical tests used in the identification of infectious agents include the detection of metabolic or enzymatic products characteristic of a particular infectious agent. Since bacteria ferment carbohydrates in patterns characteristic of their genus and species, the detection of fermentation products is commonly used in bacterial identification. Acids, alcohols and gases are usually detected in these tests when bacteria are grown in selective liquid or solid media. The isolation of enzymes from infected tissue can also provide the basis of a biochemical diagnosis of an infectious disease. For example, humans can make neither RNA replicases nor reverse transcriptase, and the presence of these enzymes are characteristic of specific types of viral infections. The ability of the viral protein hemagglutinin to bind red blood cells together into a detectable matrix may also be characterized as a biochemical test for viral infection, although strictly speaking hemagglutinin is not an *enzyme* and has no metabolic function. Instrumentation can be used to read extremely small signals created by secondary reactions linked to the antibody – antigen binding. Instrumentation can control sampling, reagent use, reaction times, signal detection, calculation of results, and data management to yield a cost effective automated process for diagnosis of infectious disease.

Epidemiology:- The World Health Organization collects information on global deaths by International Classification of Disease (ICD) code categories. The following table lists the top infectious disease killers which caused more than 100,000 deaths in 2002 (estimated). 1993 data is included for comparison.

Worldwide mortality due to infectious diseases[11][12]

Rank	Cause of death	Death 2002	% of all deaths	Death 1993	1993 Rank
N/A	All infectious diseases	14.7 million	25.9%	16.4 million	32.2%
1	Lower respiratory infections[13]	3.9 million	6.9%	4.1 million	1
2	HIV/AIDS	2.8 million	4.9%	0.7 million	7
3	Diarrheal diseases[14]	1.8 million	3.2%	3.0 million	2
4	Tuberculosis (TB)	1.6 million	2.7%	2.7 million	3
5	Malaria	1.3 million	2.2%	2.0 million	4
6	Measles	0.6 million	1.1%	1.1 million	5
7	Pertussis	0.29 million	0.5%	0.36 million	7
8	Tetanus	0.21 million	0.4%	0.15 million	12
9	Meningitis	0.17 million	0.3%	0.25 million	8
10	Syphilis	0.16 million	0.3%	0.19 million	11
11	Hepatitis B	0.10 million	0.2%	0.93 million	6
12-17	Tropical diseases (6)[15]	0.13 million	0.2%	0.53 million	9, 10, 16-18

Note: Other causes of death include maternal and perinatal conditions (5.2%), nutritional deficiencies (0.9%), noncommunicable conditions (58.8%), and injuries (9.1%).

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