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MICROBIAL ANALYSIS OF CAPSULE SHELL AND WATER IN PHARMACEUTICAL INDUSTRY: A REVIEW PAPER

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ABSTRACT

This review gives a brief overview about microbial analysis in pharmaceutical industry. In microbiology terms, pharmaceutical product capsule and water are analyse their quality and their purity purpose. Pharma studied are organized mainly with a view to making sure that the medicinal product is therapeutically advantageous and protected for the human. The evaluation is comprised the end result of microbiological purity check carried out earlier than the product are marketed. Pharmaceutical product broadly differing types are inclined to microbial contamination. Pharmaceutical product widely differing forms are susceptible to microbial contamination. In pharmaceutical industry many capsule are made and water are recognized due to fact their each day make use like industry purpose and regular purpose. In capsule, mainly observed bacteria is Escherichia coli, Salmonella spp., Shigella, and in water mainly observed bacteria is *Escherichia coli, Salmonella spp., Shigella,* and *staphylococcus aureus*. Therefore, this study investigated microbial infection of capsule and water often delivered to outpatients was analysed.

Keyword: Microbial analysis, capsule shell, Water, Microorganism

INTRODUCTION

The pharmaceutical groups are preserving the information of manufacturing and distribution as properly as the compliance departments to facilitate recalling any batch of the product from sale or provide move in case of loss of quality, however, the sustainability of the high-quality of drug treatments is publicly obscure. Several small-scalelaboratory based research evidently revealed microbial contamination in various pharmaceutical finished products such as capsule **[1]**. The microbial high-quality of pharmaceutical by way of surroundings and high-quality of the raw material used at some stage in formulation. . Manufacture process capsule reduce the viability of microbial cell significantly, hence, the microbial growth is rarely observed **[2]**. The use of contaminated pharmaceutical preparations has proved hazardous to the health of the users. There have been reports of drug-borne human infections worldwide. Microbial infection of non-sterile prescribed drugs may additionally be managed via (a) enforcement and upgrading of GMP rules; (b) manipulating physicochemical elements that have an effect on the destiny of contaminants; and (c) incorporating a preservative in the pharmaceutical formula now not for the reason of protecting horrific manufacturing practice however to make sure that the product stays high-quality **[3]**. The microbial remember in any pharmaceutical or cosmetic product can considerably have an effect on its quality via the procedure of manufacturing the product or throughout its publicity to the surroundings in day-to-day use. The final product may contain micro flora introduced from one or more sources, such as the raw materials (water), the processing equipment, the environment, the water used for the manufacture, and the manufacturing personnel **[4]**. The microbiological high-quality of pharmaceutical products is influenced by using the surroundings in which they are manufactured and with the aid of the substances used in their formulation. The presence of micro-organisms in prescribed drugs is undesirable due to the fact they can also purpose spoilage of the product and existing a contamination hazard to the customer or affected person **[5]**. Undoubtedly, the use of water in the pharmaceutical organization is indispensable, mainly in pharmaceutical liquid preparations. Not solely is water used as a factor of a number of pharmaceutical formulations, however additionally for cleansing and rinsing of clinical units and home equipment **[6]**. The techniques used and effects got ought to comply with the specs and standards outlined in the suitable pharmacopoeia. The

methods used and results obtained should comply with the specifications and criteria outlined in the appropriate pharmacopoeia. Testing, which is performed on both water and capsule, involves microbial enumeration tests for total aerobic microbial counts (TAMC) and analysis of specific pathogen, in addition to tests for the ensuing identified micro-organisms: Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, Salmonella spp., Candida Albicans **[7]**. This study is assed the microbial analysis of commercial available non sterile capsule and water for example a raw material in pharmaceutical company.

CAPSULE SHELL

Capsule, a versatile unit stable dosage shape for oral administration is designed to enclose solid, liquid or semi-solid combination of active pharmaceutical ingredient (API) and appropriate excipients in hard gelatine shells or in smooth shells of gelatine **[8]**. Capsule-based time controlled pulsatile drug delivery system has been designed and has ushered a new era in chrono therapeutics for synchronisation of drug delivery in management of diseases with circadian rhythm **[9]**. Capsules are accomplished of providing protection to encapsulated drug from deterioration induced by atmospheric oxygen, light, moisture etc. remaining to the barrier effects of shell **[10]**. The phrase 'Capsule' derived from the Latin world 'capsula', which capability a small container or container. They can be divided in most important two categories,' hard capsule' (two piece) and 'soft capsule' (one piece) in accordance with the presence of glycerol or any other plasticizer which make it tender and elastic **[11]**.

CAPSULE SHELL COMPOSITION

Gelatine: Furthermost commercially obtainable antibacterial capsules contain arrangements of colorants and opaquants to make them characteristic, many with caps and bodies of different colours.

Plasticizer: One of the greatest important characteristic of soft gel formulation is to confirm that there is minimum communication or migration between the liquid fill matrix and the soft gel shell.

Colorants/ Opacifiers: Titanium dioxide which are opcifiers and colorants important to desire in shell.

Flavouring Agent: Sugar is mainly used in flavouring agent. And also, sucrose is used in flavouring agent.

Preservatives: Ethyl vanillin, essential oils are different Preservatives.

MAUFACTURE IN EMPTY CAPSULE SHELL

Empty hard capsule shells of various fill volumes are manufactured separately and supplied ready for the encapsulation of fill formulations. The manufacturing method for the hard tablet shells is the dip molding

process, in which a set of molding pins are immersed in an aqueous answer of the movie forming polymer (gelatine or hypromellose [HPMC]) with different additives, such as a gelling agent 8and a gelling promoter (in case of HPMC capsules), an opacifier, and colorants, maintained 48-55 ºc. The molding pins with the adhering answer are withdrawn and dried at 25-35°C to shape capsule shells (body or cap). The dried body and cap components of the capsule shells are reduce to an appropriate measurement and paired to shape empty challenging capsule shells **[12]**. The bodies of hard capsule shells are filled, capped, and sealed sequentially. Unlike smooth capsules, which are one-piece, completely filled, and hermetically sealed, stuffed two-piece difficult drugs have giant headspace within. The presence of the headspace inside a challenging capsule may additionally compromise the magnificence of a product designed with an obvious shell formula and the oxidative steadiness of an encapsulated compound. The loss of fillable extent in a difficult capsule due to the headspace might also additionally end result in an exceptionally large capsule measurement in contrast to that of a smooth capsule containing a comparable fill volume. An integral section of producing liquid stuffed challenging capsules is the capability to seal the drugs correctly after encapsulation. The two most widely used methods are banding using a polymer solution (e.g., gelatine solution for banding hard gelatine capsules) and sealing using a hydro alcoholic solution **[13]**.

WATER

Water is the one of the essential commodities used by means of the pharmaceutical industry. It is broadly used as a raw material, component, **[14]** and solvent in the processing, construction, and manufacture of pharmaceutical products, active pharmaceutical ingredients (APIs) and intermediate, and analytical reagent **[15]**. It may additionally as well existing as an excipient, or used for reconstitution of products, all through synthesis, all through manufacturing of completed product, or as a cleansing agent for rinsing vessels, gear and major packing substances etc, **[16]**. There are many distinctive grades of water used for pharmaceutical purposes. Several are described in USP monographs that specify uses, perfect strategies of preparation, and best attributes **[17]**. These instructions of water can be divided into two common types: bulk waters, which are commonly produced on site the place they are used; and packaged waters, which are produced, packaged, and sterilized to maintain microbial high-quality during their packaged shelf life. There are a number of specialised sorts of packaged waters, differing in their certain applications, packaging limitations, and

different exceptional attributes. Water is the most extensively used substance, raw fabric or beginning material in the production, processing and system of pharmaceutical products. It has special chemical homes due to its polarity and hydrogen bonds. This capacity it is in a position to dissolve, absorb, adsorb or droop many extraordinary compounds **[18]**. These encompass contaminants that may additionally signify dangers in themselves or that might also be capable to react with supposed product substances, ensuing in dangers to health. Different grades of water fantastic are required relying on the makes use of and route of administration of the pharmaceutical products. Control of the fine of water at some point of the production, storage and distribution processes, together with microbiological and chemical quality, is a predominant concern. Unlike different product and system ingredients, water is generally drawn from a device on demand and is no longer concern to trying out and batch or lot launch earlier than use. Assurance of high-quality to meet the on-demand expectation is, therefore, integral **[19]**.

Non-Potable Water

Non-potable water is the water that is now not for ingesting water high-quality however which may additionally nevertheless be used for many different purposes, relying on its great **[20]**. Non-potable water is typically all raw water that is unheated, such as that system lakes, rivers, ground water, springs, and floor wells **[21]**.

Potable Water

Potable water is no longer appropriate for established pharmaceutical used due to the fact of the significant quantity of dissolved solids present **[22]**. This dissolved stable consists specifically of the chlorides, sulfates and bicarbonates of Na, K, Mg, and Ca **[23]**. A hundred ml of element of reliable water consists of no longer extra than a hundred mg of residue (01%) after evaporation to dryness on a steam bath **[24]**.

Purified Water

Purified water needs to meet the requirement for ionic and natural chemical purity and ought to br included from microbial contamination **[25]**. PW is organized via distillation, by way of ion exchange, rom water that complies with the legislation on water meant for human consumption **[26]**.

Highly Purified Water

Highly purified water (HPW) have to be organized from potable water as a minimum-quality feed-water. HPW is a special spedcation for water observed solely in the European Pharmacopoeia. This grade of water ought to meet the identical high-quality general as water for injections (WFI) together with the

restriction for endotoxins, however the water-treatment techniques are now not viewed to be as dependable as distillation **[27]**.

MICROBIAL ANALYSIS OF CAPSULE SHELL AND WATER

In capsule shell tests should be approved out before the manufacturing process is complete. Thefunction of capsule shell quality controls is to observerand if necessary, alteration of the manufacturing process in order to comply with the specification. This may include control of equipment and environment too.

The microbiological analysis of water emphasizes valuation of the hygienic quality of the supply. This involves the isolation and enumeration of organisms that indicate the presence of faecal contamination. In certain environments, the same indicator organisms may also be used to assess the efficiency of water treatment plants, which is an important element of quality control. In the microbiological analysis of water there are two different methods are used in quality control.

1) Total Viable Count

The total bacterial count is considered to be equal to the number of cfu found using soyabean-casien digest agar; if colonies are detected on this medium, they are counted as part of TBC. The total fungal count is considered to be equal to the number of cfu found using sabouraud dextrose agar with chloramphinolic; if colonies is detected on this medium they are counted as part of TFC **[28]**.

2) Detection of Pathogen

For pharmaceutical products, the European Pharmacopoeia describes sampling plans and tests for quantitative enumeration of bacteria and fungi that can grow under aerobic conditions. Enterobacter and certain other gram – negative bacteria, *E. coli, Salmonella sp., P. aeruginosa, S. aureus* are described under tests for specified microorganisms **[29]**.

DISCUSSION

In the capsule shell total viable aerobic count was small ($<10^2$ cfu/ml) which indicates the microbiological quality of the examined product was, excellent and in the specific pathogen, microorganism is absent in the capsule shell sample. So, it used in the manufacturing process in the pharmaceutical industry.

In the water analysis total viable aerobic count was different which indicates some harmful and some useful. In four water sample, Non-potable water was $<10^3$ cfu/ml which indicates that the microbiological quality of the examined product was poor while in the potable water $<10^2$ cfu/ml, purified water and highly purified water $<10^1$ cfu/ml which are indicates that potable water, the microbiological quality was good and purified water and highly purified water is excellent to the other water sample.

Table 1: Analysis of Specific Pathogen				
MICROORGANISM	**PREAPARATION**	**INCUBATION PERIOD**	**OBSERVED**	**REFERENCE**
E. COLI	**PRIMARY: MB BROTH SECONDARY: MB AGAR PLATE**	**42-44°C 24-48 HOURS 30-35°C 18-72 HOURS**	**TURBIDITY PINK COLONY OBSERVED**	**[30]**
SALMONELLA	**PRIMARY: RVSC BROTH SECONDARY: XLDA AGAR PLATE**	**30-35°C 18-24 HOURS 30-35°C 18-48 HOURS**	**TURBIDITY RED WITHOUT BLACK CENTER**	**[30]**
PSEUDOMOMAS	**CA AGAR PLATE**	**30-35°C 18-72 HOURS**	**GREENISH COLONY OBSERVED**	**[30]**
STAPHYLOCOCCUS	**MSA AGAR PLATE**	**30-35°C 18-72 HURS**	**YELLOW/WHITE COLONY SURROUNDED BY A YELLOW ZONE**	**[30]**
SHIGELLA	**PRIMARY:GNB BROTH SECONDARY: XLDA AGAR**	**30-35°C 24-48 HOURS 30-35°C 24-48 HOURS**	**TURBIDITY GRWOTH OF RED COLOURED TRANSCULENT COLONY**	**[29]**

CONCLUSION

From the above study, it can be concluded that there are exceptional sorts of pharmaceutical products which are capsule and water that are checked through specific pharmaceutical procedure. And finally result are discovered on the foundation of their quality. The pharmaceutical product capsule and water for microbial evaluation test is complies as per the pharmaceutical product of microbial evaluation test**.**

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REFERENCE

[1] Noor, Rashed; Zerin, Nagma; Das, Kamal Kanta (2015). Microbiological quality of pharmaceutical products in Bangladesh: current research perspective. Asian Pacific Journal of Tropical Disease, 5(4), 264–270

[2] C.N. Ob and U. Nwannunu, 2010. Microbiological Analysis of Drug Tablets from Selected Outlets in Umuahia, Abia State, Nigeria. Research Journal of Pharmavology, 4: 31-37.

[3] Gad, GFM; Aly, RAI; Ashour, MSE (2011). Microbial Evaluation of Some Non-sterile Pharmaceutical Preparations Commonly Used in the Egyptian

Market. Tropical Journal of Pharmaceutical Research, 10(4), 437–445.

[4] Dao, Huy; Lakhani, Prit; Police, Anitha; Kallakunta, Venkataraman; Ajjarapu, Sankar Srinivas; Wu, Kai-Wei; Ponkshe, Pranav; Repka, Michael A.; Narasimha Murthy, S. (2017). Microbial Stability of Pharmaceutical and Cosmetic Products. AAPS PharmSciTech, (), –.

[5] C Charnock (2004). The microbial content of non-sterile pharmaceuticals distributed in Norway. , 57(3), 0–240.

[6] Mwambete, K D; Temu, M J; Fazleabbas, F S (2009). Microbiological Assessment of Commercially Available Quinine Syrup and Water for Injections in Dar Es Salaam, Tanzania. Tropical Journal of Pharmaceutical Research, 8(5), 441–447.

[7] Ratajczak, M.; Kubicka, M.M.; Kamińska, D.; Sawicka, P.; Długaszewska, J. (2015). Microbiological quality of non-sterile pharmaceutical products. Saudi Pharmaceutical Journal, 23(3), 303–307.

[8] Brown S, Norman G, McNaughton A. Liquid-fill based formulation: advances and challenges. Innov Pharm Techno 2010; 10:64-8.

[9] Neeharika MS, Jeevana Jyothi B. Chronotherapeutics: an optimizing approach to synchronize drug delivery with circadian rhythm. J Crit Rev 2015; 2:31-40.

[10] Stegemann S. Hard gelatine capsules today and tomorrow. 2nd ed. Capsugel Library, Bornem; 2002.

[11] Bhavesha Rabadiya, Paresh Rabadiya; A Review; Capsule Shell Material from Gelatine to Non Animal Origin Material IJPRBS, 2013; Volume 2(3): 42-71.

[12] Gullapalli, Rampurna P.; Mazzitelli, Carolyn L. (2017). Gelatin and Non-Gelatin Capsule Dosage Forms. Journal of Pharmaceutical Sciences, (), S0022354917300783.

[13] Wittwer F. 1985. New developments in hermetic sealing of hard gelatin capsules.Pharm Manuf 2:24-27.

[14] Mehta G, Prabhu SM, Kantawala D. 1995. Industrial wastewater treatment-The Indian experience. J. Indian. Assoc. Environment Management. 22, 27 6-287.

[15] Kolpin DW, Furlong ET, Meyer MT, Thurman EM, Zaugg SD, Barber LB, Buxton HT. 2002. Pharmaceuticals, hormones and other organic wastewater contaminants in U.S. Environ. Sci. Technol. 36, 1202-1211.

[16] Stmzeski EJ. 1980. Status of wastes handling and waste treatment across the pharmaceutical industry and l97lrrfrt limitations. Proceedings of the 35th lndustrial Waste Conference, Purdue University, West Lafayette, IN. p. 1095-1108.

[17] Seif HAA, Joshi SG, Gupta SK. 1992. Effect of organic load andreactor height on the performance of anaerobic mesophilic .and thermophilic fixed film reactors in the treatment of pharmaceutical wastewater. Environ. Technol. 13, 1161-1168.

[18] Andersen DR. 1980. Pharmaceutical wastewater treatment: A case study. Proceedings of the 35s Industrial Waste Conference, Purdue University, West Lafayette. IN, p.456-462.

[19] Struzeski EJ. 1975. Waste Treatment and Disposal Methods for the Pharmaceutical Industry. NEIC-Report EPA 330/1-75-001; U.S. Environmental Protection Agency. Office of Enforcement, National Field Investigation Center: Denver, CO.

[20] Gallagher A. l954. Pharmaceutical waste disposal. Sewage Ind'Waste. 26,1355-1362.

[21] Seeler TA, Jennet JC. 1978' Treatment of wastewater from a chemically synthesized pharmaceutical manufacturing process with the anaerobic filter. Proceedings of the 33rd Industrial Waste Conference, Purdue University, West Lafayette, IN. p. 687-695.

[22] Patil DM, Shrinivasen TK, Seth GK, Murthy YS. 1962. Treatmentand disposal of synthetic drug wastes. Environ- Health. 4,96-105.

[23] Lawson J& Woldman ML, Eggerman PP. 1971. Squibb solves its pharmaceutical wastewater problems in Puerto Rico- Chem. Engng. Progress Symposium Series No. l07, "Water-1970". p. 401-404.

[24] Murthy Y S, Subbiah V, Rao D S, Reddy R C, Kumar L S, Elyas SI,Rama Rao K G, Gadgill, JS, Deshmukh SB- 1984. Treatment anddisposal of waste water from synthetic drugs plant (I.D.P.L.)'Hydqrabad, Part I - Wastewater characteristics. Indian J-Environ' Health. 26,7-19.

[25] Deshmukh SB, Gadgil JS, Subrahmanyanm PVR. 1984. Treatmentand disposal of wastewater from synthetic drugs plant (I.D.P.L.)' Hyderabad, Part II - Biological treatability. Indian J. Environ. Health. 26, 20-28.

[26] Howe RHL, Nicoles RA. 1959. Waste treatment for veterinary and

plant science research and production at Eli Lilly cfie+dLaboratories. Proceedings of the l4th Industrial waste conference,Purdue University, West Lafayette,IN, p. 647-655.

[27] Yeole Ty, Gadrl RV, Ranade DR. l966.Biological treatment of apharmaceutical waste- Indian J. Environ' Health' 38, 95-99.

[28] European Pharmacopoeia (Eur. Ph.) (2005), Microbiological examination of nonsterile products (total viable aerobic count), general chapter 2.6.12, Council of Europe, Strasbourg Cedex, France.

[29] European Pharmacopoeia (Eur. Ph.) (2005), Microbiological examination of nonsterile products (tests for specified microorganisms), general chapter 2.6.13, Council of Europe, Strasbourg Cedex, France.

[30] Q. Naveed, S. Hashmi, A. Iqbal, A. Khan Analysis of Pathogen in Nonsterile Pharmaceutical Drugs of Public Hospital of Daman (U.T). Indian Journal of Pharmaceutical Science & Research. Vol4|Issue 1| 2014 |1-3.