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MICROBIAL ANALYSIS OF TABLET AND RAW MATERIAL IN PHARMACEUTICAL INDUSTRY: A REVIEW PAPER

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ABSTRACT

Tablet is described as strong pharmaceutical dosage shape containing drug fabric usually with appropriate diluents and organized via both one compression or molding methods. Tablets stay famous as a dosage shape due to the fact of the blessings afforded, each to the producer (e.g., simplicity and financial system of the preparation, stability, and comfort in packing, delivery and provision) and the patient. Because of their composition, technique of manufacture or predicted use, tablet current a range of traits and consequently there are a number of classes of tablets. Tablet method and diagram may additionally be labelled as the system the place by means of the formulator ensures that the right quantity of the drug in the proper structure is delivered at or over the suitable time at the suitable price and in the predicted location, whilst having its chemical veracity covered to that point. Latest standards and rules canter of attention on bioavailability, bioequivalence and validation etc. affect system designing and manufacture Solid dosage forms, such as tablets, are frequent in practice. This is due to the ease of route and ride of mass manufacturing by using the pharmaceutical industry. Tablet formula contains of the energetic ingredient alongside with protecting cloth that serve a number of functions in the product. Tablets are organized on

machines regarded as presses. Material to be compressed is geared up with the aid of both dry and moist methods.

Keyword: Quality control, Raw material, Purity, Pharmacopeia's', good manufacturing practices

INTRODUCTION

The United States Pharmacopeia lists assessments to be carried out on the pill products. A description of tablets, their characteristics, preparation, and best controlests utilized to them is the concern of this quick review **[1]**.

Process validation is the key thing to guarantee the identity, purity, safety, efficacy and additionally preserving the fantastic of last product. The Process validation establishes the flexibilities and boundaries which are confronted all through the manufacturing process; the variables are managed for reaching the preferred attributes, which assures a consistency in high-quality of product during the product life **[2]**.

The vital to manage pharmaceutical strategies regardless of the problems that may additionally be addressed. Process manipulate consists of inspecting uncooked materials, controlling processes, and concentrated on for the finished product. That's why it is significant to supervise the usefulness of the technique control. In connection to this, the adaptation of the manufacturing manner have to comply with the specification as needed, which might also additionally encompass manipulate of tools and environment. Pharmaceutical merchandise in the procedure must be checked successfully for their identity, strength, quality, and purity and the merchandise are permitted or rejected by means of the nice manipulate unit in the course of the manufacture process. The highlights of this assessment are to describe nice manipulate checking out of pharmaceutical merchandise by way of the usage of extraordinary devices for the pharmaceutical industry, in accordance to pharmacopeia **[3]**.

The pharmaceutical enterprise has been main the way in the alternate of attitudes from the best manipulate (QC) to the best assurance (QA) approach.prescribed drugs has for that reason some distance been carried out solely in exceptional cases. In current years, however, it has been many times proven that microbiological manage of such merchandise is necessary. (Basel 21) Control of microbiological illness of the uncooked substances is most important, due to the fact microorganisms may also contaminate the completed product as nicely as the manufacturing plant, which would possibly reason an alternating or

everlasting air pollution of the product that is very challenging to eliminate **[4]**.

The microbial excellent of pharmaceutical is influenced with the aid of the surroundings and great of the raw material used in the course of formulation. Some ailment outbreaks have raw substances of herbal origin **[5]**. Pharmaceuticals are used in a range of methods in the prevention, treatment, and identification of diseases. In current years, producers of prescribed drugs have accelerated the nice of nonsterile prescription drugs such that these days such merchandise include solely minimal bioburden **[6]**.

The need to manage microbiological illness of all merchandise for human use and ingesting, which guide microbial perseverance and boom has been of large situation to manufacturers. Pharmaceutical and uncooked fabric for excessive microbiological requirements to shield their merchandise from spoilage on the one hand, and their buyers from infection, on the different hand **[7]**. When a product is organized in the factory, the uncooked material, which is gathered from a patient, is shipped from a clinical group that may additionally be positioned somewhere at some point of the country.

TABLET

Tablet is the most used dosage shape amongst the whole handy dosage varieties due to the fact it is easy for management, decrease charge of production, and refinement. The aesthetical first-rate like colour, texture, mouth feels, and style overlaying is relying on coating techniques. This coating technological know-how having positive hindrance or dangers to overcome this quandary **[8]**. According to the Indian Pharmacopoeia, Pharmaceutical pill are stable flat or lenticular dishes organized by using compressing a drug or a combination of drugs, with or without diluents. They fluctuate in structure and fluctuate radically in measurement and weight, relying on the quantity of administration. It is the most famous dosage from and 70% of the whole remedy are allotted in the shape of tablets **[9]**.

Among the drug that are administered orally, Solid dosage from represents the desired classification of product. Solid dosage from gives quality safety to the drug towards temperature, humidity, oxygen, mild and stress at some stage in transportation and additionally ensures accuracy of dosage, compactness, portability, blandness of test, and ease of administration. The oral drugs are normally without problems swallowed and furnish both an instant drug motion or a sustaining etc. In addition to the Active Pharmaceutical Ingredient (API), a pill formula can also comprise one or greater of the following integral parts: Diluents, binders, lubricants, glidants, anti-adherents,

disintegrating substances, colouring agents, flavouring and sweetening agents, and absorbent **[10]**.

Tablets are normally solid, proper rounded pipes, the quit surfaces of which are flat or convex andthe edges of which can also be bevelled. They can exist in different shapes comparable triangular, rectangular, and so forth also. They may additionally have strains or break-marks and may also undergo a discern or different markings. They are correctly challenging to face up to dealing with barring collapsing or breaking **[11]**.

The energetic pharmaceutical ingredient (API) molecule is the limiting thing in the improvement of a suitable formulation; hence, the manufacturing system for stable dosage varieties varies from compound to compound **[12]**.

TYPES OF TABLET

- Sub Types:

1) COMPRESSED TABLET:

Standard uncoated tablet are manufactured with the aid of compression. The standard techniques as - moist granulation, dry granulation or direct compression, are used.18 Leal (1962) laboured on "method of making a compressed tablet". This innovation requires a new manner of forming firm, smooth, and pharmaceutically elegant, compressed tablet from particulate tableting symphonies devoid of a pill die lubricant **[13]**.

❖ Multiple compressed tablet

A) Layered tablet- both two included (for two components) or three layered (for three components) tablets.

B) Compressed lined type- both pill internal a pill or pill inside a pill inside a tablet. Tablet in this classification is usually arranged for two reasons.

- To separate physically or chemically incompatible ingredients
- To produce repeat motion or extend motion product **[14]**.

2) MOLDED TABLET:

While most commercially accessible tablets are primarily prepared by solidity, tablets can also be ready by molding. Molded tablets are organised by tablet machinery or manually by forcing dampened tablet material into a mold of any shape. The formed tablet is then homeless from the mold and allowed to dry **[15]**.

TABLET OF MANUFACTURING AND PROCESSING METHODS

- Direct compression
- Dry granulation
- Wet granulation

1) DIRECT COMPRESSION

In which drugs formulations are immediately compressed from a powder

combo of appropriate excipients and API is referred to as a direct compression method. Pre-treatment of blended powder by using dry or wet granulation tissue manner is no longer necessary. It furnishes deserves ordinarily in phrases of fast production, as it requires much less machinery, decreased variety of personnel, fewer unit operations and extensively much less processing time alongside with multiplied product stability **[16]**.

Direct compression is the easiest and most economical approach for the manufacturing of capsules due to the fact it requires much less manner in than different techniques. Introduction of squirt dried lactose (1960) and Avicel (1964) had modified the pill manufacturing system and opened probabilities of direct compression tableting **[17]**.

2) DRY GRANULATION

In dry granulation manner the powder combination is compacted except the use of warmth and solvent. The two primary strategies are to structure a compact of cloth with the aid of compression and then to mill the compact to attain granules. Below two strategies are used for dry granulation **[18]**.

Present utilization of the time period "direct compression" is used to outline the manner through which drugs are compacted immediately from the powder blends of lively ingredient/s and appropriate excipients. No pre-treatment of the powder blends with the aid of moist or dry granulation is involved **[19]**.

3) WET GRANULATION

Wet granulation technique makes convenient nice grains run into severity-feed drug production. Usually, on the spot launch system is powdered with addition into nice particles accumulation an aqueous answer of a binding polymer. Controlled launch formula granulated with addition a binder polymer solution **[20]**.

RAW MATERIAL

Microbiological pleasant for raw material is one of the quintessential necessities to accomplish the 'Good Manufacturing Practices' in the Pharmaceutical Industry **[21]**. Control of microbiological infection of the raw material is most important, due to the fact microorganisms may also contaminate the completed product as properly as the manufacturing plant, which would possibly reason an intermittent or non-stop air pollution of the product that is incredibly challenging to eliminate.

Excipients are the most extensive amongst the substances in this kind of illness of treatments, considering that the microorganisms that be observed in the raw material can be the starting place of illnesses or may additionally motive spoilage of the medicaments **[22]**. The microbiological excellent of the last product (except manufacturing process)

relies upon solely on the pleasant of the beginning materials.

The range of raw material criticality assessments, the use of different indicators, and the complexity of the underlying data usually makes an evaluation of the effects generated by way of differentstudies difficult, if no longer impossible. Authors in the field have pointed out that there is a want to perceive criticality evaluation elements andindicators that grant an expanded estimation of the degree of criticality, as nicely as appropriate records sources for this motive **[23]**.

Pharmaceutical analysis for quality controal testing in pharmaceutical industry

The contrast of pharmaceutical raw material and finished merchandise for impurities and degradation merchandise is a vital section of the technique of drug improvement and production. Moreover, toxicity statistics want to be determined on any drug-related infections that symbolize an energy of greater than 0.1% of the lively pharmaceutical ingredient (API). Conventional evaluation of pharmaceutical QC and manufacturing fields has historically been carried out via titration, Identification, Loss on drying, sulfate ash, dissolution, and disintegration take a look at by way of the use of UV-Visible, HPLC, GC, or IR detection **[24]**.

Microbiological examination of Raw materials

1. **Preparation of the sample**

Dilutions of all raw material had been made aseptically with soybean-casein digest broth and the identical broth was once used to make in addition dilution Polysorbate was once brought to solubilise non-fatty water insoluble samples **[25]**.

2. **Determination of Total Viable Count by Most Probable Number (MPN) method:**

From the 1:10 dilutions of raw material (as referred to above), serial dilutions of 1:100 and 1:1000 had been organized the usage of the identical broth (3 tubes for every dilution), to get concentrations of 0.1g or 0.1ml ,0.01g or 0.01ml and 0.001gm or 0.001ml of take a look at samples, respectively. The above units of tubes had been incubated with manage (soyabean-casein broth) at 37°C for 48hours **[25]**.

3. **Tests for specified Micro-organisms:**

A dilution of the raw material in soybean casein digest broth was once used for the isolation of all particular microorganism, after incubation at 35ºCfor 5 to24 hours. In order to extend the quantity of specific microorganism current in the raw materials, appropriate enrichment broth have been used. Enrichment broths used had been Enterobacteria enrichment broth mossel for enterobacteria, MacConkey broth for

Escherichia coli, Rappaport Vassiliadis Salmonella enrichment media for Salmonella, GN media for Shigellasp. Further the isolation was once carried out the usage of the following agar media viz.,violet, crimson bile glucose agar, MacConkey agar, Xylose lysine deoxycholate agar, Cetrimide agar, Mannitol salt agar, and sabouraud dextrose agar with recognize to designated microorganism, Gram negative bile tolerant *enterobacteria, Escherichia coli, Salmonella spP, Shigella spP, Pseudomonas aeruginosa, Staphylococcus aureus* **[26]**.

Table 1: Number of viable aerobic bacteria in raw material microbial viable count

S. No.	Raw Material	Most probable number of microorganisms/ml /or/gm	References
1	Acacia	1100	[25]
2	Gelatine	>1100	[25]
3	Lactose	>1100	[25]
4	Sodium alginate	>1100	[26]
5	Starch	1100	[26]
6	Xanthan gum	>1100	[21]
7	Tragacanth	3	[21]
8	Liquid paraffin	11	[26]

Table 2: Analysis of Specific Pathogen

MICROORGANISM	PREAPARATION	INCUBATION PERIOD	RESULT	REFERENCES
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	[26]
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	[26]
PSEUDOMOMAS	CA AGAR PLATE	30-35°C 18-72 HOURS	GREENISH COLONY OBSERVED	[27]
STAPHYLOCOCCUS	MSA AGAR PLATE	30-35°C 18-72 HURS	YELLOW/WHITE COLONY SURROUNDED BY A YELLOW ZONE	[27]
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	[27]
CANDIDA	SCA AGAR PLATE	30-35°C 24-48 HOURS	CREAME COLOUR COLONY	[27]

DISCUSSION

Tablets are compacts drug transport buildings with low water content material fabric which typically come up with the cash for them specific protection in the direction of microbial contamination. Spoilage and scientific infections ensuing from microbial contamination of pills

underneath heat and humid conditions of the tropics have been pronounced **[27]**.

The enrichment raw material of each acacia and thyroxine sodium have proven solely shade adjustments from light inexperienced and boom found on Xylose Lysine Deoxycholate agar, produces faded crimson colony coloration for acacia and yellow colour colony for thyroxine sodium. The absence of attribute increase (a purple-coloured colony) and in addition confirmatory check terrible for the Prescence of Salmonella species. The enriched GN Broth proven slight turbidity for all samples, however thyroxine sodium proven greater turbidity, and boom was once current on Xylose lysine Deoxycholate agar. The colony morphology and similarly affirmation take a look at produces a bad end result for Shigella species **[28]**.

CONCLUSION

Form the above complied information it was once concluded that pharmaceutical pill can produced with the aid of three approach viz.direct compression, dry granulation and moist granulation. Out of these three methods, direct compression is the handiest and less expensive method. However, attributing to the few negative aspects of this method, we and dye granulation technique are used in modern times so as to produce fantastic tablet.

From the above studies, in all the examined raw materials, gelatine, lactose, sodium alginate and xanthan gum had larger range of microorganisms, so it wishes strict aseptic scenario at some factor of processing of uncooked materials. Thyroxine sodium, Acacia, Dried Aluminium hydroxide gel, Gelatine, lactose, liquid paraffin, sodium alginate, starch and Xanthan gum have validated growth on fully few selective media and increase used to be as soon as absent in one-of-a-kind samples. Even even although the extend used to be as soon as located in precise selective media, none of the examined samples placed to have any objectionable.

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