

Internationalization of Drug manufacturing and the Quality of Pharmaceutical products

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Abstract

The Internationalization of drug manufacture has increased day by day. As the production cost has increased, so the European countries and the rest of the world are shifting their manufacturing facilities to Asian countries like India, China etc. The Asian countries are playing a crucial role in drug manufacture (both API and Finished dosage forms). As the production increases, the quality of the product should also maintain the standards as per the regulatory requirements for human use. This article discusses the Internationalization of drug manufacture and challenges on the quality of pharmaceuticals.

KEYWORDS: Internationalization, API, Finished dosage forms.

I. INTRODUCTION

Internalization means the expansion of the business and services apart from the original origin is known as internalization. The pharmaceutical industry plays a main role which has a significant position and a strong market in the world when compared to other sectors. The manufacture of drugs is an important role in society as it is interrelated to human life. The drug manufacturer should be very careful while manufacturing a product into the market. The global pharmaceutical market in 2015 had earned the revenue of 1100\$ billion, and it is expected to achieve 1400\$ billion by 2017.

Globally the pharmaceutical market has developed, and the major pharmaceutical manufacturing countries are United States, China, France, Canada, United Kingdom, India, Japan etc.

The Indian pharmaceutical market increased 17.46 per cent in 2015 from US \$ 6 billion in 2005 and is expected to expand 15.92 per cent to the US \$ 55 billion by 2020.

The pharmaceutical manufacturers in china mainly concentrate on the domestic market. It is having around 3000 to 6000 domestic pharmaceutical manufacturers. So by these reports, we can estimate the presence of Asian countries in the pharmaceutical industry. The other countries are concentrating on investing in Asian countries because here the high manpower facilities are available and the cost of

production is too less when compared to other countries.

II. DRUG MANUFACTURING PROCESS

What is a drug- The chemical substance that has the therapeutic effects and physiological effects which is used in treatment, cure, prevention or diagnosis of a disease is known as drug.

Drug products manufacturing process: The major drug products that are manufactured across the world are Active Pharmaceutical Ingredients and Formulations.

ACTIVE PHARMACEUTICAL INGREDIENTS:

The main chemical substance that is used in the manufacture of a pharmaceutical product that has the pharmacological activity that is used in the treatment, cure, prevention or diagnosis of a disease is known as Active Pharmaceutical Ingredients.

FORMULATIONS: Drugs ready for consumption by the patients that are used or sold as tablets, capsules, syrups, emulsions, suspensions are known as formulations.

Active pharmaceutical ingredients	Formulations
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Fig.1. Mainly manufactured drug products.

III. API (ACTIVE PHARMACEUTICAL INGREDIENT) AND MANUFACTURING PROCESS

The active pharmaceutical ingredient is an active part of the pharmaceutical drug. In most of the drugs, there are usually two different kinds of chemical ingredients. The process of active pharmaceutical ingredients starts with the selection of drugs and their ingredients. The raw material that has been purchased is tested for the quality, and if it is under the specifications of standards, then the further process continues as shown below:



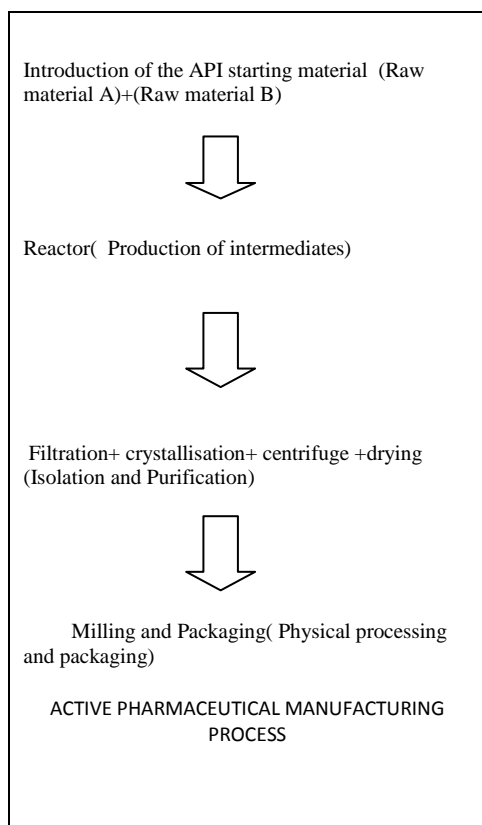


Fig.2. Example of API Manufacturing process

IV. FORMULATIONS: The drugs that are ready for consumption with therapeutic effects and physiological properties which are used in treatment or prevention of disease are known as formulations.

V. MANUFACTURING PROCESS OF A FORMULATION: The manufacture of drug products starts initially with the active pharmaceutical ingredient, and the suitable excipients are added under aseptic conditions as per the GMP standards. The following flowchart describes the manufacturing process of a formulation:

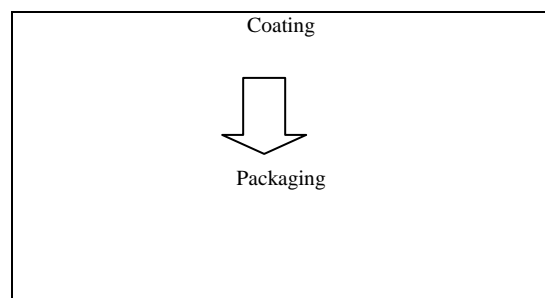
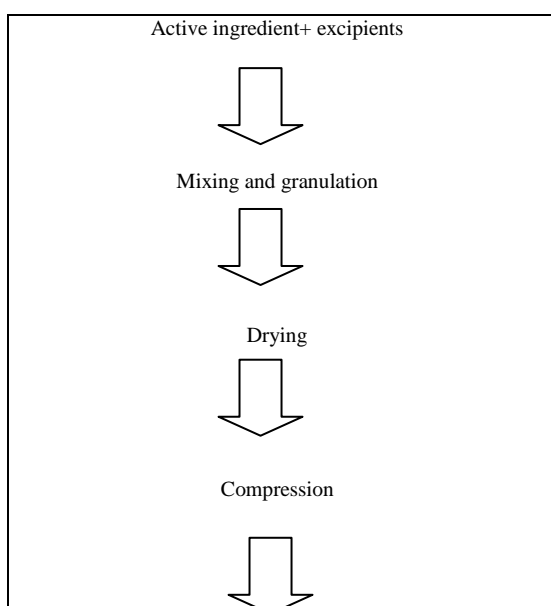


Fig.3. Example of the Formulation Manufacturing process.

Examples of formulations: PARACETAMOL TABLETS, ASPIRIN TABLETS, METFORMIN TABLETS etc.

VI. PHARMACEUTICAL QUALITY

The standard of something as measured against other things of a similar kind or the degree of excellence of something is known as quality. The quality in pharmaceutical is a major criterion for a drug manufacturer because; the life of a human is in the hands of the drug manufacturer. He has to enhance and maintain the quality throughout the process; if the quality is not maintained, here are the few examples of the incidents that happened in history.

VII. PAST INCIDENTS WHICH HAPPENED ADULTERATION DUE TO LACK OF QUALITY

[i] HEPARIN INCIDENT IN 2008:

Heparin is an anticoagulant drug. In 2008, the Food and drug administration received the reports that 19 people had died and at least 785 had experienced adverse reactions due to the contamination and adulteration of heparin drug.

The over sulphated Chondroitin sulphate closely has the same reaction as heparin, so the drug manufacturer had intensively adulterated the OSCS in the dosage form. As a result of the at least 81 deaths have been noticed as the differentiation cannot be identified by the basic test done in the laboratory, so the adulteration has not been notified. Hence the patients administered the dosage form has observed some allergic reactions, low blood pressure which leads to a fatal stroke. Finally, the products have been recalled by the regulatory authority and have questioned regarding the quality of the products.

[ii] ISOTAB- 2012

Isotab- contaminated isosorbide tablets supplied by a cardiac care clinic. Around 100 patients died, and several thousand patients hospitalized in 2012. Each of them consumed a chronic overdose of pyrimethamine every day, which caused immediate bone marrow suppression and terrible drop in platelet and white blood cell counts, ultimately leading to

their deaths. The root causes a simple mix up of an excipients and an API during manufacture.

VIII. STABILITY OF DRUGS

The stability of drugs is also a major quality factor. A drug or product can remain within specifications established to ensure its identity, quality, and purity in a specified time is known as stability.

SHELF LIFE:

It is defined as the time required for the concentration of the reactant to reduce to 90% off its initial concentration. The shelf life decides the expiry date of the product.

IX. FACTORS EFFECTING DRUG STABILITY: The primary factors effecting the stability of drug products

- pH
- Temperature
- Moisture
- Humidity
- Light
- Storage closure and containers
- Oxygen
- Particle size (suspension and emulsion)
- solubility
- Molecular binding

Some of the remedies for the factors affecting the stability:

Oxidation: The drugs can be affected by the availability of oxygen; the oxygen plays as a reactant and alters the degradation rate of the product. The remedy for oxidation is the hydrogenation of the product and incorporation of inert gas in the container.

Solubility: This is applicable to the drugs in solutions form. The stabilized by using insoluble salts of API and formulates the drug in the suspension dosage form.

X. REGULATORY REQUIREMENTS and

ICH STABILITY TESTING GUIDELINES:

ICH GUIDELINE	TITLE
Q1 A	Stability testing of new drugs and products
Q1 B	Stability testing; photostability of new drugs and products
Q1 C	Stability testing of new drug products

Q1 D	Bracketing and matrixing designs for stability testing of new drugs and products
Q1 E	Evaluation of stability data
Q1 F	Stability data package for registration application in climatic zones III and IV

XI. CONCLUSION

The Internationalization should be a part in the growth of the countries and enhance the pharmaceutical product quality and to promote the lifecycle approach to product quality and to evaluate the opportunities for innovative approaches to improve product quality throughout the product lifecycle.

The drug manufacturers should frequently review their process by internal and external audits to improve the quality of products.

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