



PROCESS ANALYTICAL TECHNOLOGY: INNOVATIVE PHARMACEUTICAL DEVELOPMENT

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Abstract:-

Food and Drug Administration's process analytical technology (PAT) initiative is a collaborative effort with industry to introduce new and efficient manufacturing technologies into the pharmaceutical industry. PAT's are systems for design, analysis, and control of manufacturing processes.¹ The Process Analytical Technology (PAT) initiative aims to move from a paradigm of 'testing quality into 'building quality in by design'. PAT tools are heavily applied in pharmaceutical workflows that underpin drug substance and dosage form development, scale-up, and manufacture.² This review introduced the concept of PAT, steps in PAT and it's applications.³

INTRODUCTION:-

Process analytical technology (PAT) is a key element of the "Pharmaceutical Current Good Manufacturing Practices (CGMPs) for the 21st Century—a Risk Based Approach" initiative announced by the FDA in August 2002 to improve and modernize pharmaceutical manufacturing.⁴ FDA is issued guidance for industry entitled: "PAT, a framework for innovative pharmaceutical development, measurement and quality assurance" in order to catalyze improvements.⁵ PAT forms a part of the Quality by Design (QbD) concept, also a regulatory-inspired methodology.⁶

WHAT IS PAT:-

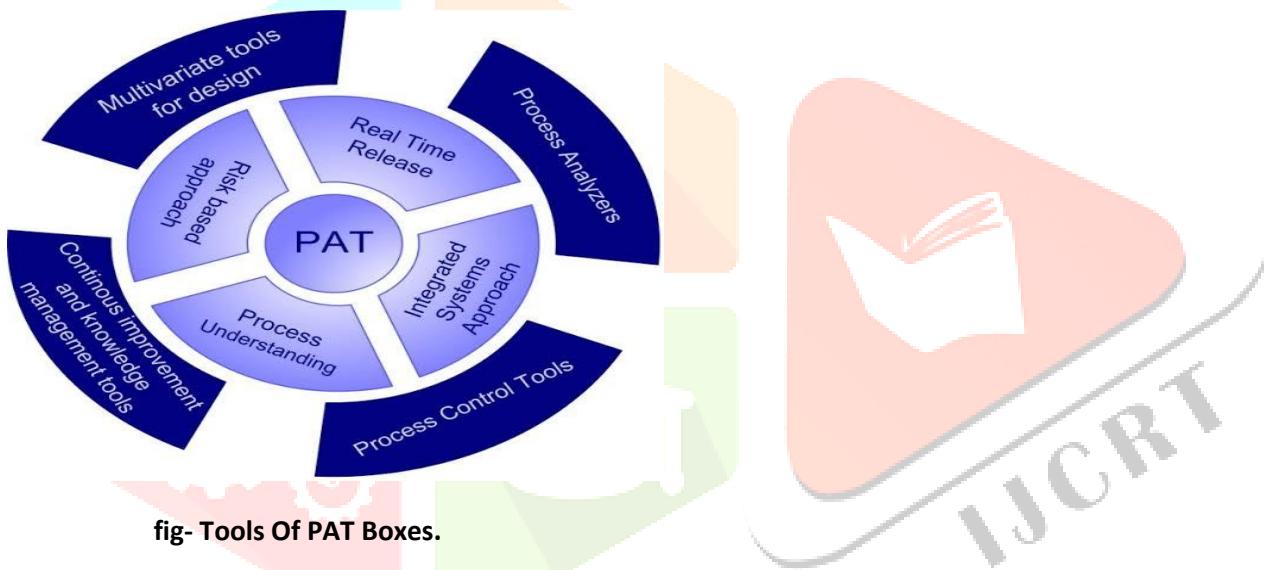
- The term "Process Analytical Technology (PAT)" has been used to describe "a system for building and control and maintaining manufacturing through timely measurements of critical quality and performance and operational attributes for active raw material and in-process materials and also processes with the aim of maintaining final product quality and manufacturing processes, as well as continuous process improvement.
- Process analytical technology (PAT) has been defined by the United States Food and Drug Administration (FDA) "as a mechanism to building, determining and control pharmaceutical manufacturing Operation through proper maintaining of Critical Process Parameters (CPP) which affect Critical Quality Attributes (CQA)".⁷
- It is important that the term analytical in PAT is viewed broadly to include chemical, physical, microbiological, mathematical, and risk analysis conducted which is an integrated manner. The goal of PAT is to enhance, understanding and maintaining the manufacturing operations, which should be consistent with the quality of drug product.⁸

ADVANTAGES:-

- Reduce the cost of manufacturing.
- If quality products is not as per specification then corrective action taken as soon as possible.
- By implementing PAT better and more stable products was obtained.
- Improve in product quality, increased regulatory compliance.
- Increased occupational safety, Decreased occupation exposure to toxic substances, Minimize and Reduced effect on environment.⁹
- Better understand the chemical and physical mechanisms, detect unstable intermediates and therefore improve the process safety.
- Improve the process robustness and the product quality.
- Hygiene conditions by avoiding sampling of highly active substances.¹⁰

PAT TOOLS:-

These tools when used within a system can provide effective and efficient means for acquiring information to facilitate understanding of process develop risk-mitigation strategies, achieve continuous improvement, and share information and knowledge. In the PAT framework, these tools can be categorized according to following:

**1) Multivariate data acquisition and analysis tools:-**

There are many different development strategies that can be used to identify optimal formulation and process conditions for these systems. The knowledge acquired in these development strategies that can be used to identify optimal formulation and process condition for those systems.

- ❖ Some manufacturers use multivariate mathematical approaches, such as the statistical design of experiments, response surface methodologies, process simulation, and pattern recognition tools, in conjunction with knowledge management systems.
- ❖ Experiments conducted during product and process development can serve as building blocks of knowledge to grow to accommodate to a higher degree of complexity throughout the life-cycle of a product.

2)Modern process analyzers or process analytical chemistry tools:-

modern process analysis tools provide non-destructive measurements that contain information related to both physical and chemical attributes of the material being processed. These measurements can be performed in the following manner:

- Offline in a laboratory

- At line in the production area, during production close to the manufacturing process
- Online where measurement system is connected to the process via a diverted sample stream; the sample may be returned to the process stream after measurement
- In line where process stream may be disturbed (e. g. probe insertion), and measurement done in real time

3) Process and endpoint monitoring and control tools:-

Following steps can be included for design a drug formulations and manufacturing process within the PAT framework:

- Identify and measure critical material and process attributes relating to product quality
- Design a process measurement system to allow real-time or near real time monitoring of all critical attributes
- Design process controls that provide adjustments to ensure control of all critical attributes.

-Develop mathematical relationship between product quality attributes and

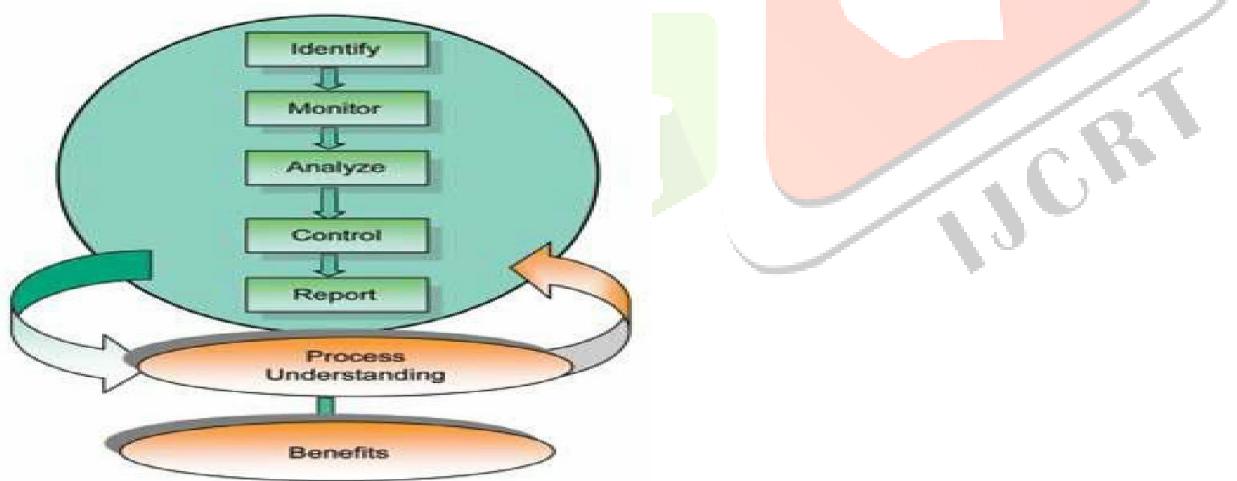
-Measurement of critical material and process attributes.

-Therefore, it is important to emphasize that a strong link between product design and process development is essential to ensure effective control of all critical quality attributes.

4) Continuous improvement and knowledge management tools-

Continuous learning through data collection and analysis over the life cycle of a product is important. Data can contribute to justifying a proposal for post-approval changes including the introduction of new technologies. Approaches and information technology system that support knowledge acquisition from such databases are valuable for the manufacturers and can also facilitate scientific communication with the regulatory agency.¹¹

STEPS INVOLVED FOR IMPLEMENTATION OF PAT:-



1) **Identify**-This step includes the process of identifying an opportunity that could benefit from the PAT approach, as well as identifying the critical quality attributes that need to be monitored and controlled in the process.

2) **Monitor**-The next step after identifying the critical quality attributes would be to monitor them. Monitoring is usually achieved using on-line instruments. The monitoring step allows us to collect data for the CQA of interest and evaluate the effect of adjusting the CQA on the overall process efficacy.

3) **Analyze**-The analysis step ensures that once we have identified our critical quality points and monitored them, we employ statistical analysis to determine how the critical quality attribute is related to the overall process efficacy. This step includes the development, verification, and validation of any statistical models that could define the process.

4) **Control**-After we have analyzed the relationship between the CQA and overall process efficacy , the next step in the

PAT effort would be to control the process to ensure that the CQA is within specified limits at all times. This is the most critical step of the PAT.¹¹

APPLICATIONS:-

1.BioPAT-

BioPAT as process analytical technology applied for development, scale-up and commercial scale bioprocess-based manufacturing of drug substances which includes production of intermediates, APIs and the final drug products. , the aim of this study is to analyze the situation in BioPAT and propose actions.¹²

2.Chemometrics-

Chemometrics is the intersection of chemistry and the mathematics of large matrices of data. Chemometrics requires the use of computers and software to perform the necessary computations. These techniques reduce large amounts of data into a few recognizable components without any loss of data.¹³

3. Other Applications-

- Examination the set of standard H₂O₂ solutions.
- vitamin B12 content of a multivitamin tablet can also be determined.
- PAT applied for end-point detection of pharmaceutical blending by combining two calibration-free methods: Simultaneously monitoring specific near-infrared peak intensity and moving block standard deviation.
- PAT is used in food analysis also.
- NIR is used in qualification of ginkgo biloba extract.¹⁴
- Quality-by-Design (QbD): An integrated process analytical technology (PAT) approach for a dynamic pharmaceutical co-precipitation process characterization and process design space development.¹⁵

CONCLUSION-

Process Analytical Technology provides better knowledge of raw materials, manufacturing parameters and their impact on finished product quality. This will result in a more robust process, better products and a huge cost savings for the manufacturer.¹⁶ PAT will encourage the implementation of innovative pharmaceutical development, manufacturing and quality assurance as well as novel analyser technologies.¹⁷ It is hopeful that the promised benefits from the PAT initiative can be reaped for both the present-day end consumer and generations to come.¹⁸

Acknowledgment-

The authors are thankful to the informants for sharing valuable information.

REFERENCE:-

- 1)Lawrence, X. Yu, et al. "Applications of process analytical technology to crystallization processes." Advanced drug delivery reviews 56.3 (2004): 349-369.
- 2)Chanda, Arani, et al. "Industry perspectives on process analytical technology: tools and applications in API development." Organic Process Research & Development 19.1 (2015): 63-83
- 3)O'Donnell, Colm P., Colette Fagan, and Patrick J. Cullen, eds. Process analytical technology for the food industry. Springer, 2014.
- 4)Rathore, A. S., R. Bhambure, and V. Ghare. "Process analytical technology (PAT) for biopharmaceutical products." Analytical and bioanalytical chemistry 398.1 (2010): 137-154.

5)Gnoth, S., et al. "Process analytical technology (PAT): batch-to-batch reproducibility of fermentation processes by robust process operational design and control." *Journal of biotechnology* 132.2 (2007): 180-186.

6)Glassey, Jarka, et al. "Process analytical technology (PAT) for biopharmaceuticals." *Biotechnology Journal* 6.4 (2011): 369-377.

7)Rakshit V Thumar, Vidhi N Kalola, Nishendu P Nadpara, Parula B Patel. A complete review of process analytical technology. *Int J Pharm Sci Rev.*

8)Goal for process analytical technology-<http://www.fda.gov/cder/OPS/PAT.html>(9 August 2012)

9)Mowery MD, Sing R, Kirsch J, Razaghi A, Béchard S, Reed RA. Rapid at-line analysis of coating thickness and uniformity using laser induced breakdown spectroscopy. *Pharm Biomed Anal* 2002;28:935-43.

10)Chimica oggi,Volume 33(2):30-33.March 2015.

11)Mali, Akash S., et al. "A brief review on process analytical technology (PAT)." *Int J Curr Pharm Res* 8.1 (2016): 10-15.

12)U.S. FDA—Guidance for Industry (draft): Analytical Procedures and Methods Validation: Chemistry, Manufacturing, and Controls and Documentation; 2000. p. 1-17.

13)Bakeev KA. Near-infrared spectroscopy as a process analytical tool. Part II. Atline and on-line applications and implementation strategies. *Spectroscopy* 2004;19:39–42.

14)Chalumeau M, Treluyer JM, Salanave B, Assathiany R, Cheron G, Crocheton N, Rougeron C, Mares M, Breart G, Pons G, Arch. Dis. Child. 83, 2000, 502–505.

15)Guidance for Industry PAT — A Framework for Innovative Pharmaceutical Development, Manufacturing and Quality Assurance.

16)Kamble, Ravindra, et al. "Process analytical technology (PAT) in pharmaceutical development and its application." *Int J Pharm Sci Rev Res* 23 (2013): 212-223.

17)A.Vishwanath,et al."Process analytical technology: Innovative pharmaceutical development, IJPBCS,Oct-Dec 2012, Volume-1,Issue-3,01-06.

18)Chew, Wee, and Paul Sharratt. "Trends in process analytical technology." *Analytical Methods* 2.10 (2010): 1412-1438.

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