



Next Generation Tools in mRNA Purification: The Role of Continuous Raman Spectroscopy Testing with Pretreatment of the Sample

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Editorial

Volume 8 Issue 1

Received Date: February 23, 2024

Published Date: March 25, 2024

DOI: 10.23880/macij-16000190

Abstract

In biopharmaceutical productions field the purification process is a crucial step in order to obtain Drugs with impurity profile according to the regulatory agency requirement. Aim of this work is to verify some relevant and recent literature and after analysis to submit to the researcher new Solutions in order to improve the global safety and the toxicological profile: is submitted a project related to the continuous testing of the purified materials using Raman spectroscopy - with pretreatment of the sample.

Keywords: mRNA; Purifications; Chromatography; Separations; Columns, Resins; Monoliths; Activated Carbon; Raman Spectroscopy; Pre Treatment of Sample; Continuous Testing Systems

Introduction

In various biopharmaceutical productive processes the final purification is a relevant step and are used in example various chromatographic processes using different systems (resins, column, monoliths).

Various materials are used for the stationary phase.

Some vials of mRNA vaccine were analyzed by independent researcher in order to verify the profile of impurity [1].

Many classic and biological drugs use activated carbon for purification of water needed (pyrogen) and in commerce there are producers that use composite materials in their

monoliths (carbon based) [2,3].

In recent times a great public debate was involved in finding of graphene like particles in some C19 vials of vaccine as well as in blood of many vaccinated people [4]. According to the regulatory agency it is accepted RAMAN spectroscopy also directly to verify impurity in the pharmaceutical product [5]. But this method (the direct one assay), when applied to Nano lipids, according to literature is not the best way to test the payload of the nanoparticle [6].

To increase the possibility to find all impurity it is crucial to pretreat the sample (Nano lipids) with solvent before performing the RAMAN test.

Material and Methods

With an observational point of view some relevant literature is reported and an hypothesis of work is then submitted to increase the global safety related some impurity for the Nano lipids based drugs production.

Results

From literature: as reported in reference form Luisetto, et al. [1-7]. "Because in various API manufacturing process are used AC products it is necessary to test the final impurity also for graphene: this is due by the different size of the particle of amorphous AC vs crystalline exfoliated graphene. (also for genotoxicity) and the toxicity that can be produced also below the threshold for impurity.

The AC production can imply really high temperature with chemico - physical change. The pharmacopeia monography for AC not cite the word graphene" [8].

Experimental Project Hypothesis

In order to increase the power of detecting impurity in Nano lipids drugs it is necessary at the end of the production process to test in continuous way the final product using RAMAN spectroscopy (with pretreatment of the sample). In this way only after use of solvent t is possible to avoid the interference played by the Nano lipids.

Discussion

In Literature is Reported

- The crucial role played by the purifications steps.
- Various chromatographic procedures are used, using resins and monoliths.
- Some producers use activates carbon composite materials.
- For production of water for injectable (Pirogen) are used also charcoal filter systems membrane.
- The test for PAT (Proces Analytical Technology) analysis in pharmaceutical production use also Raman Spectroscopy.
- It is allowed by regulatory agency the direct testing whit RS (without pretreatment with solvent of the sample).
- This method is not the best to test the payloads for Nano lipids drugs. According Vanden-Hehir S, et al. "A major advantage of Raman is that it allows direct imaging of the Nano carriers, and not the payload en-capsulated within them."
- Independent researcher finded graphene like particle in some vials of some C19 vaccine [1].
- Other researcher finded graphene particle in blood of

vaccinated [4].

- From membrane of activated carbon can be released impurity.
- One method to produce water for injection (pirogen remove) is using activated carbon.
- (The same in order to remove pirogen from injectable).
- Activated charcoal is produced also using really high temperature and it can exfoliate graphite and graphene [8] even if under the threshold requirement of the regulatory agency.
- In monography of activated carbon of various pharmacopeia the term graphene is not reported.

Conclusion

For all reported in discussion i is opinion of the authors that to increase the level of safety in mRNA Production and purifications it is necessary to test the final product in biopharmaceutical production in continuous way using a Raman Spectroscopy with pretreatment of the sample with solvent. This to avoid interference played by the Nano lipids.

Also for the classic chemical drugs and their productive process it is of interest to verify the absence of impurity form activated carbon membrane used related the level today admitted (thresholds) by pharmacopeia.

What are the toxicological effect played by some impurity if present in drugs final product also under the regulatory thresholds?

The m RNA purifications steps can be improved using new technology, classic chemical analytical tests whit pretreatment of the samples and performed in continuous way.

Conflict of Interest

No

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