EDITORIAL

Graphene and derivates: Physico-chemical and toxicology properties in the m-RNA vaccine manufacturing strategy needed specific proof of absence for the regulatory aspects

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ABSTRACT

Observing the fact that every year various registered and authorized drugs are recalled by the public regulatory agency (in example last Ranitidine cases due by the possibility of impurity presence of a cancerogenic sustantia) it is interesting to observe the innovative production strategy of some m RNA vaccine.

Also for the bio- technological drugs product the regulatory agency ask quality standard for impurity for the obviously safety implications.

The biotechnological drugs, as the classic chemical drugs, due by the complex manufacturing process use raw material and industrial procedure that require.

Great quality monitoring according the GMP normative rules. So it is no too strange to discuss of impurities in this new kind of products and also for the covid-19 vaccine.

Keywords: Graphene; Covid -19; m-RNA, vaccine; Side effects; Toxicology; Chemistry manufacturing technology and Materials, contaminations; Impurity.

INTRODUCTION

This work start by recent and really interesting new evidence (DISINFECTION and Natural Docet Dark field microscope analysis n 1/ 2022) and other research works published also by university professors and other professionals. (CAMPRA P university of ALMEIRA , YOUNG R O , YOUNG Mi. LEE et al, GIOVANNINI F et al).

Before of all it was done a review of interesting article related the chemical-physical and toxicological property of graphene derivates (also woks published before the Covid-19 Pandemic) as well as distribution profile related the way of sub ministration.

It was also analyzed ADR characteristics' that some recent Covid-19 vaccines have reported in the pharmacovigilance center (national and international).

Great attention was done towards the verification of the manufacturing technology used in field of m-RNA vaccine since form the research in oncology.

From literature Graphene and Grafene Oxide GO and other derivates are subject of many uses in bio- technological research: in diagnostic field but also in production and especially in last decades.

It is possible to report Carrier or adjuvant or extractive property (there are study that show increase in immune response after their use), and object of research for INTRA NASAL covid-19 vaccine.

Properties to improve RNA extraction- purification in manufacturing field. (Absorption property, increase RNA stability)

In some literature are described uses of pegylated Nano lipids whit graphene oxide.

In m-RNA Vaccine research development. (Some producers can provide this raw material and the technical and security sheet are easy available on internet).

On literature as well as by bio-technological producers there are various products made of MAGNETIC MICROBEADS used for extraction of RNA derivates.

These are all use known at today and easily verifiable in biomedical database since not suspicious times [1-23].

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Interesting also to note as there is also a preprint written by the CEO of a great pharmaceutical industry that produces innovative covid-19 vaccine and other researcher of the same industry report among the reagent for production of a covid-vaccine per non-human primate's magnetic micro beads. (See reference on article under publication as reported).

(And on literature are reported article works about graphene GO - magnetic micro beads) [24-42].

MATERIALS AND METHODS

With an observational point of view some relevant literature is analyzed in order to produce a global conclusion related the topics of this work [43-50].

RESULTS

We have performed as a review part on searching activity on biomedical database like Pub med and other in order to find relevant literature for this work.

All using keywords useful to limit the references to only the crucial ones in order to cover the various arguments: independent researcher results in findings graphene like particle in some vials of covid-19 vaccine, or related the chemico -physical properties of this class of compounds, ore the biotechnological use in bio-pharmaceutical production.

As we have seen: In literature also before COVID-19 pandemic various researcher published works Related the role of graphene derivates in example to better purify m RNA vaccine production (also for oncologic research), as carrier, or as adjuvant and also recently studied for intranasal flu vaccine new products.

In last decades this innovative material was introduced in various settings and also in biomedical or in biotechnology (in example for testing – biosensor, tissue regeneration, antibacterial properties and other).

Because this product can increase extraction property of m-RNA in manufacturing bio-pharmaceuticals as showed by researcher (about 170% vs. classic methods according Xuan-Hung Pham et al using magnetic beads) it is relevant to verify if some producers of raw material Use this technology.

So it is Necessary to verify the impurity level for raw material and also in the final biopharmaceutical products (Using a right analytical chemical methods: with pretreatment of the sample with solvent in order to extract - before to test the analite from Nano lipids particles avoiding interferences in the cases of m RNA vaccine nlp).

This because the toxicity profile of this class of products require deeply investigation. (Rare severe ADR like thrombosis, myocarditis, pericarditis)

The fact that some regulatory agency after GMP visit in production site asked officially to the final producer of some m RNA VACCINE to complete the quality

Profile of some excipients tells us to more clarify this aspect. To confirms this proposal there are the evidence collected in some university as in some research study reported (Turin university-chemistry faculty, Campra p.-university of Almeria professor chemical science).

Regarding the contaminants it is of interest to report they in 26 August 2021 BBC news Coronavirus pandemic Japan suspends 1.6 million Modern doses over contamination fears A staff of Japan's supermarket group Aeon receives a dose of the Modern vaccine "Japan has suspended the use of about 1.63 million doses of the Modern vaccine due to contamination.

A metallic substantia that react with magnetic field in some lots of interest finally to remember two recent Italian judge sentential: PISA E FIRENZE 2022 it was recognized in one cause- effect relationship between a covid-19 vaccination and a Thrombocytopenia reaction in an 16 years old, and in the other case the judge written that this vaccine are experimental, DNA invasive, potentially of irreversible effect and not prevedile at today.

Even if this drugs are officially registered by regulatory agency during the last years.

In example some countries restricted uses of some covid-19 vaccine in determinate subpopulation even initially not done.

The same some technical sheet was recommended to be updated by EMA PRAC introducing some Rare ADR not present in the first approved VACCINE one or also changed the name of the vaccine in order To update registrative documents reporting new contraindications.

For this reason it is necessary that regulatory agency official asks to the producers to verify in official way the presence and absence of graphene derivates in the final products using qualitative but also quantitative methods (with control).

And the results must to be certified for all lots released.

Last version of European pharmacopeia allows the use of Raman spectroscopy.

For production quality control scope and also as non-destructive methods – direct.

But independent researcher used a classic destructive methods using solvent to pretreat Nano lipids in their analytical procedure to find graphene presence in vials of vaccine m -RNA.

The different results obtained by regulatory agency (ABSENCE) and by some independent researcher (PRESENCE OF graphene like particle) need a better verify.

According to a Personal opinion of a university full Professor PhD chemical science received (24-08-2022)

"In my opinion GO and other non-declared substances must be located by microscopically techniques coupled with spectroscopy (Raman, XPS, e diffraction).Otherwise the analyses will yield negative identification, as their amount is low and they show as dispersed particles"

Experimental project hypothesis

In order to verify the absence/presence of graphene derivates in vials of some bio- pharmaceutical compounds it is needed to test 100 sample of a new technological products (In example m RNA vaccine in Nano lipids).This using analytical procedure officially CGMP approved (RAMAN spectroscopy) and with the acceptable sensibility. (One procedure with a classic destructive method and using also a nondestructive method).

1) Method as approved EUROPENA PHARACOPOEIA like direct nondestructive method

2) Method as reported by some researcher (with extraction in a classic chemical method before test, destructive method).

This sample must divide in group of 20 and send blinded to various and different accredited chemical laboratory and independent.

It is needed a control group, all sample blinded.
The sample must to be treated for the pre-analytical need (extraction) before to be analyzed.
This in order to verify in the same condition the inside Nano lipids included and outside of this.
Results: verify is there is or not significative presence of graphene or its derivate in the final approved vials. ($p< 0,005$)
The results must to be divided using a destructive method and a non-destructive one.

DISCUSSION

So related to all of this , matching the evidence of some test on vials of vaccine as well as research on dark filed microscopy and related the fact that the toxicological profile of this particles seem to correlate with the ADR reported (rare thrombosis, pericarditis and other).
Also the chemico-physical properties of these particles are so peculiar and make possible to give explanation of some phenomena.
According the authors it is clear that it is needed to deeply investigate this evidence verifying the manufacturing technological process in order to clear if is presence or not possible pollutants residues of production even if this are not declared and reported on official technical sheet and registered by public health authorities. (In the raw materials, reagents of final product).
The pharmaceutical producers use often to buy raw materials form other producers.
The same author submit to the researcher to analyze a more wider and significative number of vials of the various vaccine for covid-19, thought various and certified independent laboratory and using the blind technique.
To confirm this proposal there are the evidence collected in some university as in some research study reported (Turin university-chemistry faculty, campra p.-university of Almeria professor chemical science).
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CONCLUSION

As global conclusion it is possible to ask to the innovative vaccine producers to provide official written proof of chemico-analytical absence of graphene and derivates in the final vaccine product.(the same by the international regulatory agency).
The same to provide full clarification of the bio-technological manufacturing process. Even if there are patent of industrial secret

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