

The role of mechanical engineering in the development of nano drug delivery systems; a review

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Abstract

The pharmaceutical area can present some opportunities for mechanical engineers to develop a vast type of dosage forms particularly novel forms like nanoparticles. The classical education of mechanics needs some alterations to prepare appropriate education courses in this regard. In order to present some views about this issue, we collect some information around the importance of mechanical engineering in the designing of nano-based drug delivery systems. A review process was performed using *National Center for Biotechnology Information (NCBI)* by means of MeSH keywords such as mechanical engineering, pharmaceutical dosage form, drug delivery system, nanoparticles and nanotechnology. The searches included full-text publications written in English, published in PubMed central over a 10-year period (2006-2016). The abstracts, reviews, books with no experimental data as well as studies without explicit involving of mechanical engineering in the designing of drug delivery systems were excluded from the analysis. The reviewed literature revealed that there is good progress in application of mechanical engineering in the designing of nano-based drug delivery systems in recent years. However, more clinically and *in vivo* attempts are needed in this regard. This information may present some beneficial views for graduate students as well as academic curriculum designers about the importance of mechanical engineers in pharmaceutical area.

Keywords: Drug delivery system; Mechanical engineering; Nanoparticles; Nanotechnology; Pharmaceutical dosage form.

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INTRODUCTION

Traditionally, pharmaceutical industries have not benefited from innovative engineering solutions or new ideologies of mechanical and chemical engineering. For years, drug products were manufactured manually, affecting the quality of the final product. Over the years, interest grew in the safety and quality of medicinal and pharmaceutical products, together with decreasing the cost of products by applying more structured science-based manufacturing methods [1, 2]. Besides, there is an essential need to increase the efficacy of a drug and simultaneously decrease

its side effects. Therefore, finding a method to aid drugs to mainly reach into their target side in the body is necessary. Drug delivery is the proper strategy for administering and delivery of drugs in an efficient way. To achieve such discipline, different specialists from chemists, biologists and engineers can play a very helpful role. In recent years, engineers, chemists, and pharmacists attempt to formulate active pharmaceutical ingredient into products with novel and more efficient abilities [3, 4].

For years, theoretic and practical mechanics have shown progressive methodologies for

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investigating the engineering systems which are used in the medical, transportation, materials, defense, and energy industries. In recent years, applying mechanic approaches for developing medical and biomedical processes holds excessive potentials. The exciting role of mechanical engineering in the design of drug delivery systems is an outstanding opportunity to develop novel and efficient pharmaceutical and medical products. This contains common pharmaceuticals such as medicines, biopharmaceuticals, and consumer businesses such as exporting medicines [3-5].

The development of nanotechnology over the recent decades has promoted a big movement in drug delivery. Nanoparticles are ultrafine particles with nano-range dimensions in diameter, prepared from any type of biocompatible substances. They can improve the properties of materials, as compared to similar bulk materials. For instance, they have a higher surface-to-volume ratio than macro-scale objects. Identification and application of these outstanding properties motivated researchers to manipulate the chemical and molecular structure of novel nanomaterials and tailor them to profiles required for a wide range of applications [6-10]. The combination of biology and medicine with mechanics by means of nanotechnology led to a new and efficient field of technology. The target delivery of therapeutic agents by designing drug delivery systems was presented in the 1950s [5, 11-13]. Basically, the transportation of nano-scale objects inside the body follows the general mechanical laws of transport. These objects can include biological objects such as protein, or synthetic ones such as chemotherapeutic agents, contrast agents, or drug-loaded nanoparticles [14, 15]. Target-delivery aspects can be achieved by transporting drug-loaded nanoparticles with precise engineering properties. Mechanic instructions can also be used for developing new methods or strategies for preparing drug delivery systems. Delivery systems, e.g. nanoparticles, nano-machines, and nano-robots may also benefit from mechanic approaches [5, 11, 16-21]. The nano-mechanic field can be applied as a potent tool for nanoparticles' preparation, transportation, and internalization, as well as drug release from nanoparticles or designing different types of delivery carriers.

In this report, we illustrate the importance of engineering knowledge in nano drug delivery systems through a collection of some articles in

the field. The review process was conducted in *National Center for Biotechnology Information (NCBI)* using MeSH keywords such as mechanical engineering, pharmaceutical dosage form, drug delivery system, nanoparticles and nanotechnology.

EXPERIMENTAL

Search strategy

A review process was performed in the *National Center for Biotechnology Information (NCBI)* using MeSH keywords and their combinations, e.g. mechanical engineering, pharmaceutical dosage form, drug delivery system, nanoparticles, and nanotechnology.

Search Criteria

The search was limited to studies with full-text articles in English, published over a 10-year period (2006-2016).

Scientific and medical abstracts, reviews, books/book chapters with no experimental data were excluded from the analysis.

Studies without the explicit involvement of mechanical engineering in the design of delivery systems were excluded from further investigation.

Data screening process

After applying the initial exclusion criteria, data screening was performed in two stages. The first stage included the use of EndNote 7 software for removing the duplicates, and the second stage was performed by reading the abstracts.

RESULTS AND DISCUSSION

The electronic search provided 278 titles. After removing the duplicates, this number was decreased to 200 titles. Among them, 97 papers were relevant to the present study's goals. The stages of search strategy are summarized in Fig. 1 and Table 1.

According to collected papers, novel drug delivery systems like nanoparticles have reported to show two key issues; the methods to developing drug delivery systems and to recognize the transport mechanisms of drugs in delivery systems. The related articles define the recent progresses in developing drug delivery systems or devices. Then, considering these issues and based on the reviewed papers the collected titles can be categorized into two main topics; 1) Topics related to the study of nanoparticles'

preparation, transportation, and internalization, as well as drug release from nanoparticles or designing different types of delivery carriers using mechanic processes, and 2) topics related to the design of devices or procedures which can be used to develop nanostructures or improve their administrating route by means of mechanic laws.

Among the finally screened papers, 58 titles were related to the use of mechanic laws in studying nanoparticle transportation and internalization, drug release from nanoparticles, or designing different types of delivery carriers. For example, Agarwal *et al.* investigated the internalization and shape-specific uptake mechanisms of hydrogel nano-discs in mammalian cells. This study presented fundamental information on nanoparticle uptake using mechanic laws in different mammalian cells, the importance of nano-scale geometry, designing improved nano-carriers, and predicting nanomaterial toxicity. According to their results, mammalian epithelial, endothelial, and immune cells preferentially internalize disc-shaped, negatively charged hydrophilic nanoparticles of high aspect ratios

compared with nanorods and lower aspect-ratio nanodiscs under *in vitro* conditions.

Additionally, kinetics, efficiency, and mechanisms of uptake are all shape-dependent and cell type-specific [18]. Moreover, Ahmad *et al.* presented a report on the use of micro-scale and nano-scale structures for drug delivery applications using an electric field. They revealed that the designing process of the drug transporter as well as the release mechanism can be controlled by changing the physical state of the component containing the active agent [28]. In addition, Ali *et al.* tested the reprogramming of cellular phenotype by soft collagen gels. Their results indicates that soft collagen gels can induce cellular phenotype and cytoskeleton organization in an extraordinarily different way compared to a classical synthetic polyacrylamide hydrogel cell culture model and can be applied as a new functional biomaterial to design drug carriers [29].

Furthermore, Castro *et al.* reported the mechanical design of DNA nanostructures as a rapidly developing area with a great potential for applications in drug delivery and templating molecular

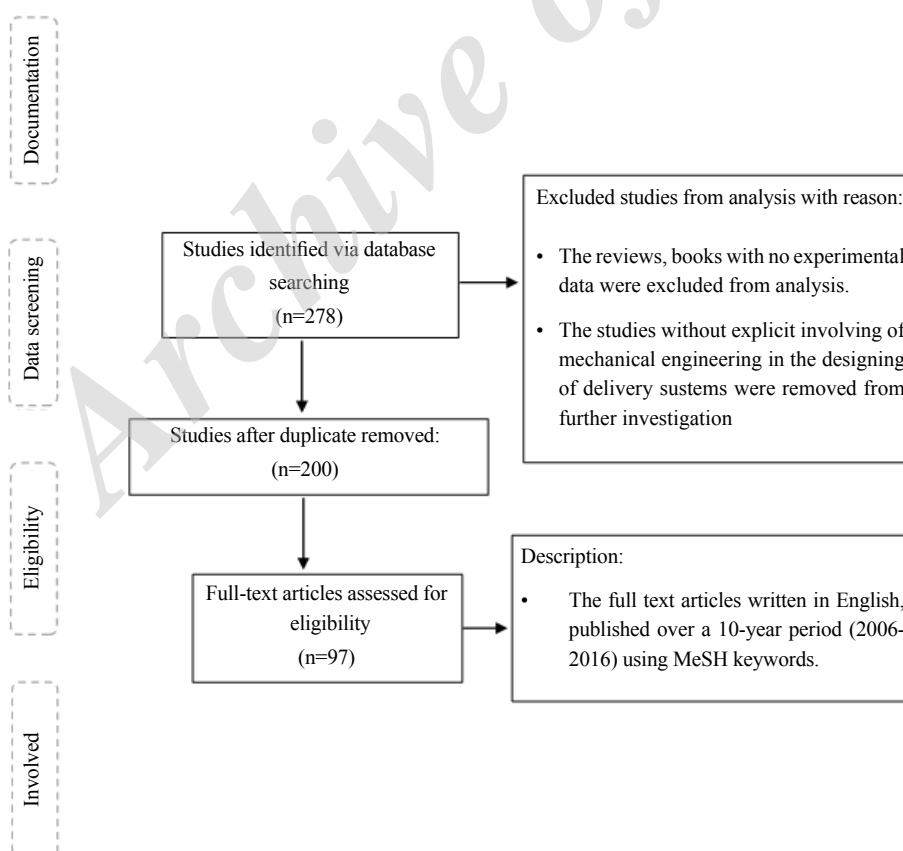


Fig. 1: Stages of search strategy.

Table 1. Stages of search strategy and definitions for MeSH keywords.

MeSH keywords and their combinations	Definitions for MeSH keywords	Number of MeSH	Number of full-text journal articles in PubMed
mechanical engineering	The practical application of physical, mechanical, and mathematical principles [22]. The science of designing, building, or equipping mechanical devices or artificial environments to the anthropometric, physiological, or psychological requirements of people who will use them [23].	2	61763
pharmaceutical dosage form	Completed forms of pharmaceutical preparation in which prescribed doses of medication are included. They are designed to resist action by gastric fluids, prevent vomiting and nausea, reduce or alleviate the undesirable taste and smells associated with oral administration, achieve a high concentration of drug at target site, or produce a delayed or long-acting drug effect [24].	1	110452
drug delivery system	Systems for the delivery of drugs to target sites of pharmacological actions. Technologies employed include those concerning drug preparation, route of administration, site targeting, metabolism, and toxicity [25].	1	79080
nanotechnology	The development and use of techniques to study physical phenomena and construct structures in the nanoscale size range or smaller [26].	1	55705
nanoparticle	Nanometer-sized particles that are nanoscale in three dimensions. They include nanocrystalline materials [27].	7	124670
mechanical engineering in designing pharmaceutical dosage form	-	-	45
mechanical engineering in designing drug delivery systems	-	-	228
mechanical engineering in designing pharmaceutical nanoparticles	-	-	5
Total	-	-	278
After removing the duplicates	-	-	200
After data screening	-	-	97

components. They offered a new suggestion about the foundation of mechanically active nanomachines which can generate, transmit, and respond to physical cues in molecular systems [30].

Other papers (39 titles) were related to designing devices or procedures in order to develop nanostructures or their administrating route by means of mechanic laws. Baumgartner *et al.* employed an extrusion process based on mechanic procedures as a promising tool for continuous manufacturing of solid nano-formulations [13]. The design of bio-microfluidics for tissue maintenance, drug release, mechanical support, and cell delivery [31] or, similarly, the preparation of dissolvable micro-needle arrays for intradermal delivery of nanoparticles for dry delivery to skin microenvironments were also reported by Domachuk *et al.* and Bediz *et al.*, respectively [32].

The collected papers showed that compared with the being of good efforts development of drug delivery systems and devices, reports on the transport mechanism of drugs in delivery

systems are rare. Among the investigated papers, Gowrishankar *et al.* reported how electrical fields facilitate drug delivery by creation of microholes or nanoholes in the skin [33] and Pua and Zhong described the cavitation mechanisms in ultrasound-based drug delivery [34]. Nanoparticles and nano-based drug delivery systems have unique and sometimes unknown properties and therefore, there is a need to eager the scientists especially mechanical engineers to design more project on transport mechanism of these systems. Lacking of clear considerate about different physiological events (existence of enzymes, barriers, etc) affect the performances of a drug and therefore studying of carrier systems will not be successful. For example, a delivery system for cancer targeted delivery need to overcome some complex complications such as the unwanted absorption by other cells or tissues and the penetrating from tumor micro-vessel walls or different cell surfaces [4].

The search results showed that despite of an increasing growth in the application of mechanical

engineering for developing new pharmaceutical delivery systems, there are rare clinical and *in vivo* attempts in this area. Among the investigated papers, as an *in vivo* attempt, Namdee *et al.* evaluated vascular-targeted spheroidal particles for imaging and drug delivery applications in atherosclerosis [32]. Indeed, the human body is not as simple as a cell culture or a mechanical device. Besides, due to complicated properties of nano-based drug delivery systems, prediction of the general problems of drug delivery in the body is not possible only using *in vitro* methods [4]. So, there is an essential need to design *in vivo* examinations by different scientist especially engineers.

CONCLUSION

The present study aimed to collect useful evidence from the scientific literature regarding the role of mechanical engineering in designing nano-based pharmaceutical delivery systems. A review was performed on the *National Center for Biotechnology Information (NCBI)* using MeSH keywords. The review of papers revealed that there is considerable growth in the application of mechanical engineering in designing and developing new pharmaceutical delivery systems. However, the search results showed that there are rare clinical and *in vivo* attempts around this subject. Nanoparticles have complicated and sometimes unknown properties and therefore there is an essential need to design *in vivo* examinations by different scientist especially engineers to see the overall problems of a drug delivery system as well as its mechanism of action in the body.

Future viewpoint

The role of mechanics in medicine and particularly drug delivery areas needs major alterations in the educational programs of mechanic students. The classical education of mechanic (involving of fluid and solid mechanics) should be merged with courses of biology, chemistry and pharmaceutical nanotechnology to attain a basic understanding of biological processes. This can lead to more potent role of mechanical engineers in developing novel drug delivery systems such as nanoparticles.

CONFLICT OF INTEREST

The authors have no conflict of interest.

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ETHICAL STATEMENT SECTION

The authors declare that there are no ethical issues for human and animal right.

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