

## Pharmacy or PharmaNBIC: Thinking about 50 years ahead of pharmacy today<sup>+</sup>

Amir Azadi<sup>1,2</sup>, Mohammad Hossein Morowvat<sup>1</sup>, Amirhossein Sakhteman<sup>3</sup>, Abdolali Mohagheghzadeh<sup>1,4,\*</sup>

<sup>1</sup>Pharmaceutical Sciences Research Center, Shiraz University of Medical Sciences, Shiraz, Iran.

<sup>2</sup>Department of Pharmaceutics, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran.

<sup>3</sup>Department of Medicinal Chemistry, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran.

<sup>4</sup>Department of Phytopharmaceuticals (Traditional Pharmacy), School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran.

<sup>+</sup>This article is a Festschrift for more than half a century of honest and effective efforts of Professor Hassan Farsam in pharmacy education.

### Abstract

The contemporary trends and concepts in pharmacy are widely affected by the emergence of Nano-, Bio- or Info- technologies (NBI) as an attempt to develop different principles of medicine. This commentary is trying to make a think tank room for 50 years ahead of today's pharmacy, where the ambience of pharmacy will be affected by such technologies together with cognition (NBIC) to achieve intelligent, low adverse reaction and holistic action medicals. *Keywords:* Biotechnology, Cognition, Information technology, Nanotechnology, NBIC, Pharmacy.

### 1. Introduction

Designing a prompt prospect for the future 50 years is an inevitable feature of efficient systems. Great developments in many aspects of pharmaceutical sciences, along with other sciences, have impelled the scientific community to explore ways to equip themselves for the next future (1). An overview of the future in different fields of medical sciences brings this fact in to the mind that contagious diseases will be in the era of extinction. On the other hand the prevalence of non-contagious diseases such as cancer and neurological disorders will reach a culmination point twice as before. The world population will also increase widely adding to the problems of human in the future (2). It is therefore of great importance to improve all trends of pharmaceutical sciences based

on the future prospect of the world.

In the recent years, exploring a convergence between different branches of science attracted many interests as a main concept. Nano-, Bio-, Info-technologies and cognitive science (NBIC) have been taking important roles in augmenting the human quality of life and have been therefore represented as the NBIC project (3). An ancient description of NBIC can be explained as the four philosophical elements; earth, water, wind and fire (4). Where earth denounce for structural features, water for life aspects, wind for connection pattern and fire for cognition concepts. While the application of any of the NBIC fields by its own can make new prospects in pharmaceutical sciences, also a pair or three combinations of these sciences can make new basics in pharmacy. Finally the combination of all of these sciences can lead to a unity in the science.

In the following Commentary, we try to elucidate the contribution of NBIC separately or

*Corresponding Author:* Abdolali Mohagheghzadeh, Department of Phytopharmaceuticals (Traditional Pharmacy), School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran  
Email: mohaghegh@sums.ac.ir

as a whole in the next future of pharmacy.

## 2. Nano-technology in Pharmacy

There are many definitions for Nano-technology at the time being; The most known one based on Nano-technology institution is defined as the research and development of technologies at atomistic levels, molecules and macro molecules at 1 to 100 nm scales. This technology will lead to knowledge in the area of phenomena and materials at Nano-scales. The systems and structures based on this technology are beneficial to increase the quality of human life. These features of Nano based preparations are due to their particle size and the identity of the systems. Briefly speaking, Nano-technology is the world at Nano- scales and behaves beyond those events seen in reality. The materials can exhibit different features compared to those at normal size dimensions, and this is because in nanotechnology they are converted to Nano-size scales (5). These features will lead to materials with more tightness, conductivity, adjustable optic parameters, porosity, electrical insulation, super paramagnetic and less corrosive properties. Nano materials are able to cope with some hard to treat biological problems. During the past decade, many efforts have been conducted in the area of targeted drug delivery in nano particulate systems. On the other hand, this approach has to deal with many challenges in order to increase its efficiency. Based on some hypotheses, nano carriers keep their nature during circulation inside the body. In a report published in Nature Communications (2014), it was stated that the architecture in Nano-systems is controlled by processing methods (6). It was shown that the Nano-carriers with the size of 75 nm, can deliver the entire drug molecules directly into the tumor cells. On the other hand, an increase of particle size to 150 nm, leads to the splenic and hepatic accumulation. Therefore, particle size and particle size distribution can have a major impact on Nano-carrier biofate. Nowadays, the researchers have a significant approach towards fabricating and utilizing the smaller particles for drug delivery purposes. Several drug delivery systems based on nano-technology have been presented to the global pharmaceutical market until now (Table 1). For instance, Daunoxome<sup>®</sup>, Cycloset<sup>®</sup>, AmBisome<sup>®</sup>,

Doxil<sup>®</sup>, Emend<sup>®</sup>, Diprivan<sup>®</sup>, DepoCyt<sup>®</sup>, Megace ES<sup>®</sup>, Myocet<sup>®</sup>, Rapamune<sup>®</sup>, Vivagel<sup>®</sup>, Triglide<sup>®</sup>, Tricor<sup>®</sup>, Combidex<sup>®</sup> are the FDA approved nano-formulations utilized to manage the various diseases that are hard to treat. The nanoparticles will be replaced by the particles in picometer dimensions in the next future. Undoubtedly, the pharmacokinetic and bio-distribution and overall biofate of these very small particles are different from the previous generations. This opportunity may conduct the future therapies to the modification of gene sequences and also structural molecules. This approach can alter the future drug definition.

## 3. Bio-technology in Pharmacy

During 1980s, biopharmaceuticals were considered as therapeutic proteins which were produced using recombinant DNA or hybridoma technology in the case of monoclonal antibodies. However, this nomenclature appeared inadequate in 1990s after the development of gene therapy, invention of antisense technology and aptamers as the first nucleic-acid based therapeutics (7).

Today, a biopharmaceutical is considered as a therapeutic agent based upon proteins or nucleic acids which are used for pharmaceutical and medical application, prevention or in vitro diagnosis of diseases. Its production includes some procedures, except direct extraction from its natural tissue or its unengineered form. Based upon this, recombinant proteins, monoclonal antibodies which are used for therapeutic applications and also nucleic acid based therapeutics are considered as biopharmaceuticals.

The first generation of biopharmaceuticals, were mainly the “simple replacing proteins” which had a similar amino acid sequence compared to its naturally existing form in the human body. They were administered in order to replace or reinforce the natural proteins in mankind. However, nowadays a large number of newly emerged biopharmaceuticals are engineered to enhance their pharmacokinetic properties, lowering their immunogenicity or producing fusion proteins which are called the “second generation” of biopharmaceuticals (8).

Synthetic biology, although was coined in 1978 as a new scientific term to indicate the recom-

binant DNA technology, but it did not gain global attention. In the beginning of 21st century this scientific term was reintroduced as unnatural molecules which mimic the function and performance of their natural counterparts. In a broad view this area of science includes disassembly of the natural networks and nodes in a biological circuit and its redesign. Hence, this field of study deals with changing and redesigning the existing natural metabolic networks. In this roadmap, some new born sciences including systems biology and different -omics data seem to be useful to create novel networks, self-renewing elements and novel biological organism from non-living materials which have never existed before (9). The first approved stem cell-based therapy product (Holoclar®) has attained new promises for the next biotechnology-based therapeutics (Table 1) (10).

Bio-Cogno in pharmacy is a well-established concept which is defined as pharmaceutical Bio-cognition. The distinctive feature of this technology is firstly, defining the natural relation-

ship between the elements in a biologic system and redesigning/ reshaping the current features. In this context, development of a novel generation of therapeutic vaccines (e.g. synthetic vaccine viruses), novel engineering methods for genome engineering (Fomivirsen based upon antisense technology and newly emerged CRISPR CAS method), the first approved gene therapy product (Alipogenetiparvovec (Glybera®) (11), are some examples for this growing area of study. Besides, the creation of first fully synthesized bacterium, *Mycoplasma laboratorium* (Synthia) warrants an interesting and multi-potential technology which needs novel regulatory and ethical laws (Table 1).

#### 4. Info-technology in Pharmacy

Different branches of bioinformatics including different -omic technologies are applicable in pharmaceutical sciences. Using structural bioinformatics in the prediction of the biological activities for the synthesized compounds have been described in many studies (12). Obtaining a

**Table 1.** Basic knowledge and incoming merged concepts in pharmaceutical science.

| Science             | Related fields in pharmacy         | Pharmaceutical class/Examples  |
|---------------------|------------------------------------|--|
| Nano                | Pharmaceutical nanotechnology      | Daunoxome®, Cycloset®, AmBisome®, Doxil®, Emend®, Diprivan®, DepoCyt®, Megace ES®, Myocet®, Rapamune®, Vivagel®, Triglide®, Tricor®, Combidex®           |
| Bio                 | Pharmaceutical Biotechnology       | mAbs: Avastin®, Herceptin®/ Aptamers: Macugen®/Stem cells: Holoclar®/ Vaccines   |
| Info                | Bioinformatic/Pharmacometrics      | Pharmaceutical Softwares: PSN™, Xpose™, PopED™   |
| Cogno               | NF                                 | NF   |
| Nano-Bio            | Biopharmaceutical nanotechnology   | Adagen®, Abraxane®, Aurimune®, Elestrin®, Epaxal®, Estrasorb®, INGN 401®, Neulasta®, Oncospar®, Pegasys®, PEGIntron®, Somavert®                          |
| Nano-Info           | Nanoinformatic                     | NF   |
| Nano-Cogno          | NF                                 | Rate-preprogrammed drug delivery systems; Activation-modulated drug delivery systems   |
| Bio-Info            | Bioinformatic                      | Raltegravir  |
| Bio-Cogno           | Systems biology/Genome engineering | Fomivirsen/Synthetic vaccine viruses, <i>Mycoplasma laboratorium</i> (Synthia)/ CRISPR CAS/Oriental traditional medicine/Alipogene tiparvovec (Glybera®) |
| Info-Cogno          | Artificial intelligence            | NF   |
| Nano-Bio-Info       | NF                                 | Feedback-regulated drug delivery systems; Site-targeting drug delivery systems   |
| Nano-Info-Cogno     | NF                                 | NF   |
| Bio-Info-Cogno      | NF                                 | NF   |
| Nano-Bio-Cogno      | NF                                 | NF   |
| Nano-Bio-Info-Cogno | NF                                 | NF   |

NF: Not found in the literature; TM: Trade Mark.

3D-protein ligand interaction fingerprint (PLIF) is a useful strategy in designing specific drugs with more potency and less side effects (12). Raltegravir (Table 1), is an example of computer based drug design studies. Time dependent molecular dynamic simulation studies provide a huge amount of information for the stability of ligand protein complexes (13). A developing approach in information technologies is artificial neural network and fuzzy logics which is a hybridization of cognition and Info-technology. The application of artificial intelligence is well observed in many quantitative structure activity relationship studies. The result of these studies could be a promising prospect for rational drug design in future decades (13).

The increasing prevalence of neurological disorders is directing many drug design studies towards this field. An inherent of nanotechnology and informatics is a new science called nano-informatics. This science could provide valuable suggestions in design and application of responsive drug delivery systems. A metamorphosis in the syllabus of pharmaceutical sciences is therefore needed to accommodate the novel sciences in pharmaceutical industry. As it is clear, in future, the modeling of novel drug delivery systems, especially nano and biotechnology-based formulations is the important global scientific approach in this area. On the other hand, combination of Info-, Bio- and Nano- technologies, presents a unique opportunity to describe and predict the cellular behaviors and subsequent related malfunctions via the precise mathematical models and software such as PSN<sup>®</sup> and Xpose (Table 1).

## 5. Cognition in Pharmacy

Assuming that atomic and molecular structures are involved in nanotechnology, biological behaviors are taking role in biotechnology and connection is observed in information technology yet the area of research involving cognition which is not yet technologic, is more ambiguous. What we anticipate from cognition is the set of all mental abilities and processes related to knowledge (14): attention and concentration, memory and working memory, judgment, evaluation, reasoning and computation, problem solving as well as decision making, comprehension, and produc-

tion of language etc. Cognition can be considered at higher levels with respect to other NBI topics and can lead to intelligent systems in cases where it is combined with other NBI subjects. The emergence of cognition in pharmacy goes back to pharmacists' attempts in obtaining knowledge of medicinal plants known as "pharmacognosy", for the treatment of different maladies. For this purpose the practitioner needed a specific type of "gnosis" towards the herbal potentiality. Although cognition has a historical contribution in the field of psychology, converging cognition with medicine may result in a more holistic view to medical treatment and new representation of human requirements for each ailment would be presented. The convergence of holistic and reductive approaches together with systems approach is so informative (3). Nowadays such approaches are followed by societies like International Society of Psychoneuroendocrinology. By the way, the knowledge flowing in neuroscience fields can have impressive effect on utilizing cognition in different aspects of applied science, especially pharmaceutical topics. In this area, neurophilosophy which is the philosophy of neurons' functions (15, 16) is so enthusiastic.

There is no report of medicine which is directly derived from cognition in the literature. However, the result of utilizing cognition in medical sciences can be summarized as bellow:

- Systems, equipment or pharmaceutical agents with the capability of intelligently activating parallel mechanisms throughout the body without side reactions.
- Biosensors and indicators for evaluating and adjusting the medication, according to the stage of the disease.
- Development of pharmaceutical agents to the holistic function medicinals is expected with pharm-robotic function.
- Medical ethics will be more predominant and consequently philosophy, ethics, rights and law principles will be more apparently demanded than before.

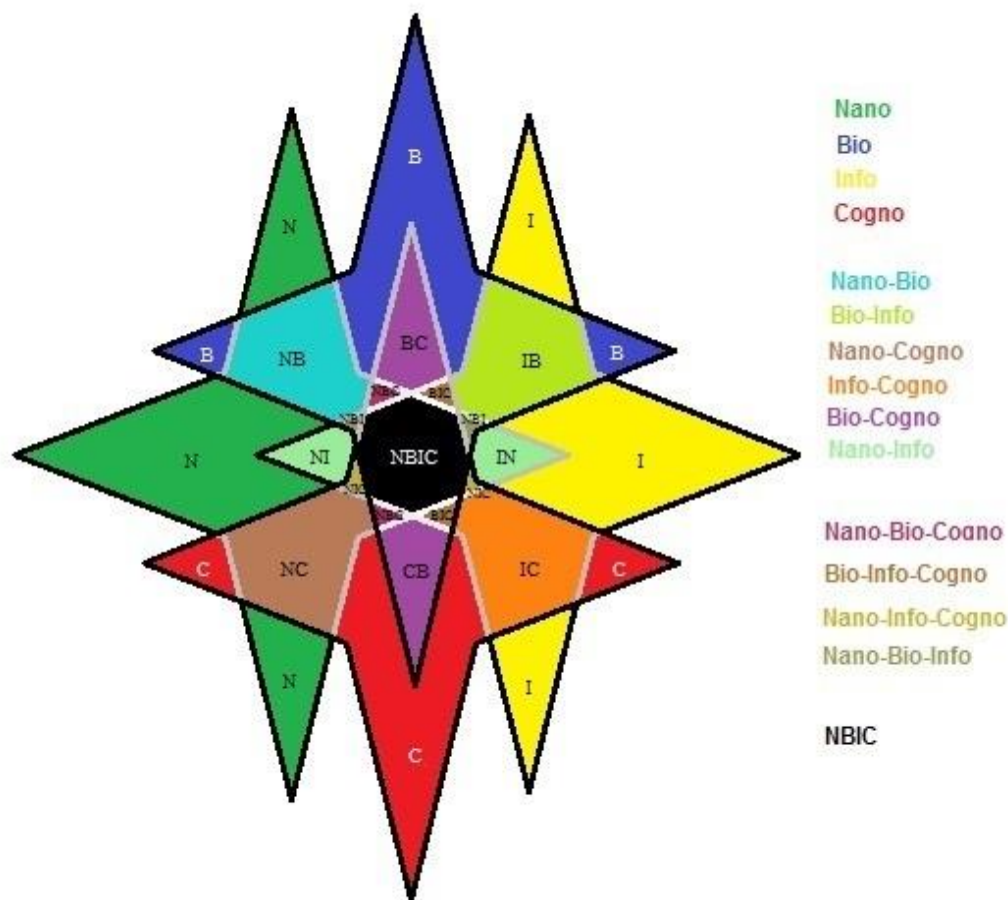
## 6. PharmNBIC

The convergence of NBIC can lead to versatile hybrid technologies. These technologies can

be constructed in different ways of two, three or four combinations with 15 diversities (Figure 1). For instance nanotechnology is the study of the structures at nano dimensions. Merging it with other fields can lead to different particle dimensions that improve penetration as well as novel conceptions for the systems. For example in the biopharmaceutical nanotechnology field (i.e. the merging of Bio- and Nano-technology), there are several FDA approved novel pharmaceutical formulations such as Adagen<sup>®</sup>, Abraxane<sup>®</sup>, Aurimune<sup>®</sup>, Elestrin<sup>®</sup>, Epaxal<sup>®</sup>, Estrasorb<sup>®</sup>, INGN 401<sup>®</sup>, Neulasta<sup>®</sup> etc which are available in pharmaceutical market. Also, Nano-informatic can be a good example for combination of nano and info technologies (Table 1).

Bio- features are in correlation with life,

motion and biological compatible fundamentals inside the living organisms. Merging it with other fields can lead to Bio-informatic and systems biology and also genome engineering. The Info-features are the connections and velocity as a consequence of modeling different parameters inside the system. Merging it with other fields can lead to artificial intelligence as the combination of Info- and Cogno-. The Cogno- which has not emerged as an independent technology can lead to artificial intelligence and conscious functions. For instance Nano-Cogno in pharmacy could be well defined by pharmaceutical Nano-Cognition. A new approach towards this technology can be the development of systems in order to intervene in the treatment procedure by means of Nano- based systems. This means that the trial and error experiments will be



**Figure 1:** Schematic view of fundamental sciences (NBIC) and 15 possible combinations.

replaced by a more comprehensive view of the body, diseases and Nano-particles. In other words, the perspective of this system is responsive systems with automatic behaviors at Nano-scales. In this regard, rate-preprogrammed nanostructured and activation-modulated nanostructured drug delivery systems may be the good illustrations for this concept. Also, feedback-regulated and site-targeting drug delivery systems are the suitable examples of Nano-Bio-Cogno combination in pharmaceutical sciences. To the best of our findings, there are trade mark medicines and related accessories that have been presented in Table 1.

## 7. Perspectives

To establish a proper future program for the next 50 years of pharmacy, it is worth considering the precious decades' achievements of pharmaceutical sciences in all fields. Since 1920, the basics of pharmaceutical research have been the synthesis and biological evaluation of small molecules. The research approach changed to target based systems since 1950 and continued to 2000 and designing biological systems emerged after the year 2000 (17). It seems that the NBIC-based approach could be the next research approach in the 2050s. Therefore what seems to be vital in order to avoid uncontrollable burst of knowledge in this field are:

- Establishing pharmacy think tank headquarters inside universities and related organs in education, research, production and control systems in the field of PharmaNBIC.
- Pharmacy programs (5, 10, 20 and 50 years) according to PharmaNBIC should be proposed for research, education and production in such headquarters.
- Auguring educated pharmacists and allied specialists to establish new knowledge based companies on NBIC concept.

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- Making suggestions to decision makers for the convergence of pharmacy basic science syllabuses towards converging sciences (e.g. psychoneuroendocrinology).
- Auguring new departments and related journals to PharmaNBIC
- Convergence of Cogno- and philosophical issues with pharmacy to prepare a holistic picture of pharmaceutical sciences, as it has been described earlier for medical sciences (18).
- Considering the human rights and prerogatives based on NBIC concepts
- Concerning daily reports of Nano- and Bio-technologies' warnings, specialized organizations need to be established for training the strict and in detail control systems, considering biosafety issues and ecosystem concerns, as well as managing the possible dangers of NBIC technologies even far, before well establishing PharmNBIC.

The convergence of all these sciences will lead to unity in science and a renaissance in trends in pharmaceutical sciences that will thereafter appear as the concept of "Shefa" in oriental believes. Actually, we will cope with a wonderful Aladdin lamp story. A genie like NBIC concept which is more vigorous than its accompanying sciences could be deduced. "What wouldst thou with me? I am a slave of the ring and will obey thee in all things".

## Authors' Contribution

Amir Azadi has arranged the nanotechnology and related parts. Mohammad Hossein Morowvat has prepared biotechnology, systems and synthetic biology materials. Contribution of Amirhossein Sakhteman was in the sections related to bioinformatics. Contribution of Abdolali Mohagheghzadeh was in cognition, perspectives and total overview of the manuscript.

## Conflict of Interest

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