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Modern Medicine and Pharmaceutics

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1. Introduction

There are evidences that people have been using medicine to cure illness from the early civilization in Africa, Asia and Europe. The wide varieties of treatments such as Shamanism, surgery and drug formulations have been practiced. The drug materials from the plants, animals, minerals were used for the medicinal purposes, are referred today as “Crude Drugs”. As knowledge on disease and drugs is expanded further and more purified form of the materials were chosen to prepare further effective drugs and medicines. As the development of modern societies immersed in the world, two different philosophical approaches in the field of medicinal treatment came forward. In the Eastern societies such as in China and India, holistic approaches were adopted. In these societies, disease or illness is considered as an integral part of the body and can be corrected with the selected foods or formulation of crude drugs mainly derived from plants and a few from animals or minerals together with the body adoption. But in contrast, in the Western society, disease is considered as the separate entity from the body and can be eliminated by surgery or using particular chemical substance. Especially in the western medicine, the practice of using purified form or pure chemical substances is developed. The knowledge on chemical sciences especially synthetic chemistry and purification techniques were rigorously developed to fulfil the need of chemical substance. This led to not only the foundation for the development of science and technology but also the concept of industrialization came forward.

In general, pure chemical substance is not administered directly to the disease condition to cure or treat the disease. Depending on the disease condition and chemical nature of the drug substance, several kinds of formulation and route of administration are in practice. Therapeutic effect of the drug substance will only be achieved, if the right chemical substance with sufficient amount be delivered in the targeted tissue sites for the sufficient length of time in the person having pathophysiological condition. Formulations play great roles in distributing drugs in the body. Moreover, according to the type and condition of the disease, same drug substance might provide separate therapeutic effects based on the types of formulation, route and interval of administrations. In general, the term ‘drug’ represents pharmacologically active chemical substance. Pharmaceutical sciences provide the
knowledge and technique to utilize the drug substance for the effective therapy. In recent years, because of the advancement in pharmaceutical sciences, several drug substances are better utilized for the health benefit. Pharmaceutical industries contributed enormously for the advancement of modern medicine together with the development of particular the formulation for desired route of administration in order to obtain optimum therapeutic value of the drugs substance.

2. Historical overview on the development of modern drugs

In fact, many of the drug substances which are used today commercially have certain historical links to the traditional uses. Among them, the history of morphine and acetyl salicylic acid (aspirin) are widely discussed and well documented.

There are evidences of using latex of opium plant (*Papaverum somniferum*) in Chinese traditional medicine, Ayurveda, and Ancient Greek medicine to relieve pain. The desire to obtain more effective and purer drug has always been remained as the deep thrust in human nature. The first report of morphine purification was made by Derosne in 1803 and further detail was published by Seguin in 1814. (Derosne, 1803; Seguin, 1814). A German pharmacist, Sertürner claimed the first purification of active compound from opium latex and published in 1805, later it was found that the isolated compound was not an alkaline narcotic component rather it was identified as meconic acid (Sertürner, 1805; 1806). On continuing, Sertürner extracted the opium poppy latex with hot water and precipitated with ammonia and obtained a pure crystalline compound having narcotic properties of opium (Sertürner, 1817). The compound was named as morphine (1) and structure was confirmed later. In 1874, Wright reported heroin (2), a diacetyl derivative of morphine (Wright, 1874), and it was commercialised by Bayer AG in 1898. Because of the strong narcotic properties, heroin was banned for the therapeutic use but morphine and codeine (3), another derivative of morphine, are still very important commercial drugs today after almost 200 years of their discovery (Figure 1).

![Morphine and Derivatives](image)

**Fig. 1.** Structure of morphine and its derivatives.

After extraction and purification of morphine, the technique was applied to isolate other important alkaloids and they were commercialized immediately. In 1817, Pelletier and co-worker reported emetine (4) from *Ipecacuanha* and strychnine (5) from *Strychnos* (Pelletier, 1817). In 1820, same group reported the isolation of quinine (6) from *Cincona* species (Pelletier, 1820) which was commercialized as the anti-malarial drug. Other important alkaloids such as brucine (7) and caffeine (8) in 1819, colchecin (9) in 1920, codeine (3) in 1833, atropine (10) in 1848 were isolated (Nicolaou & Montagnon, 2008). The complete structures of many of these compounds were confirmed later. Conine (11) was isolated in
Fig. 2. Structure of alkaloids having therapeutic and commercial uses. Discovery of these alkaloids led to the foundation for the modern medicine and industrialisation.

1826, complete structure was elucidated in 1870 and later synthesized in 1881. All these drugs with almost of 200 years of history are still used in commercial scale (Figure 2) (Newman, 2010).

Another important modern drug with long history and widely discussed molecule is acetyl salicylic acid (aspirin) (13). In spite of development of several effective antipyretic drugs the importance of aspirin has never been diminished.

Acetylsalicylic acid (13), an acetyl-derivative of salicylic acid (14), is a mild, non-narcotic analgesic. It is useful in the relief of headache and muscle and joint aches. The drug works by inhibiting prostaglandins production which sensitizes nerve endings to pain. The discovery of aspirin (13) is linked to 14, salicyl aldehyde (15) and salicin (16), a chemical component derived from the bark of Willow tree.

Fig. 3. Structure of aspirin and other related compounds. Salicin, a compound isolated from the bark of Willow tree led to the discovery of aspirin.
4.6 Multifunctional pharmaceutical nano-carriers drug delivery

Drug discovery is very expensive and time consuming process. In addition to this, it is not sure that the successful candidate will appear at the end. Therefore the research on development of drug, especially the delivery system to enhance the bioavailability will make more fruitful therapeutic outcome. The development of new drug-delivery technologies also made the existing drug more useful. In the present book, the nano-carrier as delivery system is discussed in brief.

Nano-carrier drug delivery is mainly focused to those drugs which are potent pharmacologically but it could not be utilized fully because of toxicity (side effect) or less efficacy due to low bioavailability. In general, less soluble or less permeable drugs can not reach to optimum concentration in the systemic circulation. Therefore these classes of drugs are easily packed into the lipid nano-particles in the form of liposome or micelle. Because of the drug encapsulation inside the lipid molecule cluster, the physical properties of the drug molecules dominated by the lipid cluster particle and therefore lipid molecule cluster serves as nano-carrier and drug molecule can be delivered to the targeted site. Nano-particle of lipid encapsulated with drug molecules can easily be solubilised and penetrated into the cell.

There are already several drugs based on nano-carrier delivery formulations. A good example of nano-carrier delivery is liposomal formulation of amphotericin B. Amphotericin B has a broad spectrum of activity and is a drug of choice for life threatening invasive fungal infections, including disseminated candidiasis, aspergillosis and protozoal infection affecting the internal organ (Viscerel leishmaniasis). However, its use is compromised by associated adverse side effects.

But because of nano-carrier delivery liposomal formulation three products such as AmBisome (a small unilameller liposomes formulation with the size of 80 nm, composed of hydrogenated soy phosphatidyl choline, cholesterol, disteroyl phosphatidyl glycerol and amphotericin B in a 2:1:0.8:0.4 molar ratio with α-tocopherol), Abelecet (composed of amphotericin B, dimyrystoyl phosphatidyl choline and dimyristoyl phosphatidyl glycerol in a 1:1 drug-to-lipid molar ratio with sizes is up to 1.6-11 μm) and Amphotec (containing amphotericin B in a complex with cholesteryl sulphate at a molar ration (1:1) with the particle size of 100-140 nm) are commercialized. Lipid-based nano-carrier formulations are found to be superior in clinical efficacy.

Based on the lipid type and physical condition, the size of particles, nature of the particles can be designed. In addition one or more desired ligands can me inserted to drug encapsulated nano-particle which allows the drug molecule to be delivered into the targeted sites in controlled manner. The additional ligands might be monoclonal antibody (binds to specific site), polyethylene glycan (remains longer time in circulation), binding with heavy metal (allows to trace the particle), cell penetrating peptide (allows the particle to penetrate into the cells), DNA binding (allows the DNA to be delivered) and magnetic nano-carrier (to trace the particles) (Figure 10).

These one or more ligands can be incorporated in the same particles therefore multifunctions of nano-carriers can be achieved together with the delivery of the drugs. Already
the first generation of multifunctional nano-carriers is developed. For example, the nano-carrier type (B+C) having immunospecific and PEG ligands, should have ability to carry the drug molecule to the immunospecific cells where ligand binds and deliver the drugs and PEG allows the nano-carrier to remain longer hours in the systemic circulation (Figure 11).

The future medicine will be the nano-particles packed with several ligands which will be able to carry the drug molecules to particular targeted cell with monoclonal antibody and penetrated the cell membrane and required drug can easily be delivered without interfering with the circulatory system and other tissues or biomolecules (Figure 12). Such smart drug delivery will reduce the side effect and enhance the drug efficacy. This will be the foundation of ‘Intelligent Therapeutics’ of future drug formulation.

Fig. 10. Diagrammatic representation of nano-carrier designed for the pharmaceutical purpose. 

A: Traditional nano-carrier; B: Targeted nano-carrier (Immunospecific); C: Long circulating nano-carrier (PEG protected); D: Contrast nano-carrier (for imaging); E: Cell-penetrating nano-carrier; F: DNA-carrying nano-carrier; G: Magnetic nano-carrier.
Fig. 11. Diagrammatic representation of first generation multifunctional nano-carriers.

Fig. 12. Dream multifunctional nano-carrier.

5. Conclusion

Happy life, healthier life and long life have been remained as the goal of human life philosophy. Modern medicine, at least in a part, contributed to humanity to become more prosperous and more civilized. In fact, in searching of more effective medicine in the quest of healthier and longer lives, it led to the development of basic chemistry and human biology. The traditional agricultural based human demographical society transformed to industrialisation and pharmaceutical industries have great role for the globalization of the world. Moreover, modern medicine discovery and development not only supported to healthier and longer life but also encouraged to prosper the development of the modern science and technology.

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From the dawn of civilization, humans have been dreaming of happy, healthy and long-life. Our life expectancy is twice longer than 100 years ago. We know more about the diseases. Therefore we have developed new drugs to fight against them. The demand for drugs was so high that we developed Pharma industries. Although Pharma industries took responsibility of producing the needed drugs and gave us a quality of life, misuse of drugs brought further complication. Therefore, discovery, production, distribution, and the phase of administration of patients' quality assurance has to be controlled with a technological procedure and tight regulations to make the system as effective as possible for the benefit of human health. Our book provides selected but vital information on the sources, tools, technologies and regulations regarding the current status of medicine development.

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