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Review Article

Innovative medicines, technologies and approaches for improving patients' health care

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ABSTRACT

Despite remarkable scientific and technological achievements during the 20th century, the 21st century has already witnessed additional new and profound changes in all areas of medical science and research, including innovations and discoveries in biology, cellular biology, genomics and proteomics, pharmaceuticals, medical devices, and information technology. This review is an up-date on some of the existing therapies, drug delivery technologies, and approaches that aimed to improve patients' health care and quality of their life.

K**ey words:** Recent drug discoveries, recent drug therapies and technologies, pharmaceutical care, waves of change in pharmacy, international trends in pharmacy education

INTRODUCTION

Especially in the developed world, the average human life span is hovering around 70 years and is projected to increase. This increase in average age is largely due to developments in the pharmaceutical industry and improving healthcare [1]. Biomedical innovations including advances in medicines, medical procedures, and public health have provided extraordinary benefits to the public. Currently, pharmacists are involved in the management of pharmacotherapy in clinical scenes more extensively than they did ever. Including but not limited to patient-care system; clinical pharmacy specialization has begun to develop in population-based health roles and in systems management as well and patients themselves have played a critical role in propelling advances by focusing attention on the urgency of developing therapies and spurring creative approaches, and by participating in clinical trials. No doubt that the development of pharmaceutical education also plays a significant role in developing the health industry and pharmaceutical care of the patients [2, 3].

Recent Drug Therapies, Discoveries and Technologies: An Overview

1. **Genomic Technology:** Recent advances in genomics, proteomics and computational power present new ways to understand human disease at the molecular level [4].
   1.1. **Pharmacogenetic Testing:** The term pharmacogenetics comes from the combination of two words: pharmacology and genetics. Pharmacology is the study of how drugs work in the body and genetics is the study of how characteristics that result from the action of a single gene or of several genes acting together are inherited and how they work in the cells of the body. Therefore, pharmacogenetics is the study of genetic factors that influence how a drug works [5]. Wide individual variations exist in the expression and function of CYP450 enzymes. Research shows genetic variation, or polymorphism, in these enzymes is one of the most important causes of variable drug response. These variations result from single nucleotide polymorphisms (SNPs). Depending on the genetic makeup of the CYP450 enzyme system a person has inherited, the metabolic activity of a particular CYP450 enzyme can be categorized as poor, intermediate, extensive, or ultra-rapid. Correspondingly, some people are considered normal metabolizers of drugs, others are intermediate metabolizers, still others are poor metabolizers (experiencing no clinical effect from the drug), and some are ultra-rapid metabolizers (experiencing toxic drug effects). Understanding this can help tailor drugs in the future best suited for a particular individual (personalized medicine) or group [6, 7, 8, 9].

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1.2. Recombinant DNA (rDNA): The development of safe and effective new therapeutics is a long, difficult, and expensive process. Over the last 20-30 years, recombinant DNA (rDNA) technology has provided a multiple of new methods, molecular targets and DNA-based diagnostics to pharmaceutical research that can be utilized in assays for screening and developing potential biopharmaceutical drugs [10, 11, 12].

1.3. Gene Therapy: Gene therapy involves the insertion of genes into a patient's cells and tissues with the intention of treating a disease or condition. One current focus of intense research is in using gene therapy to treat hereditary diseases such as muscular dystrophy, cystic fibrosis or hemophilia, where a defective gene or, more correctly, mutant allele is replaced with a functional one. The first approved gene therapy procedure was carried out in 1990 on a very young patient with a disease known as severe combined immunodeficiency [13, 14]. In the procedure, the missing gene was inserted into white blood cells which were then infused into the patient's bloodstream. A carrier, known as a vector, must be used to transport the therapeutic gene to the desired target cells and sites and a commonly used vector is a genetically modified virus in which any harmful genetic material has been removed and the desired gene incorporated. Various biomolecules also lend themselves to use as vectors. The vast majority of gene therapy research is focused on somatic cells (which comprise most of the cells in the body). While it is possible to modify germline cells, this remains *an ethically contentious area.* Nanotechnology may play an important role in future development of gene therapy, for example in designing new types of vector like dendrimers that can be constructed to carry DNA or RNA and targeted to cells with a high level of specificity and low toxicity [15].

1.4. Short Interfering RNA (siRNA) Delivery: The field of RNAi and siRNA therapeutics has made significant strides in the past decade toward clinical applications. In the future, synthetic cationic materials, including lipid-based molecules and polymers, should continue to play an important role in the safe and efficacious delivery of siRNA [16, 17, 18]. Future developments will require an attention to the immunostimulatory potential of siRNA and the modification methods that can be used to engineer siRNA that does not activate the innate immune system. Delivery continues to pose the most significant barrier to the clinical use of RNAi therapeutics, and future work centering on the development of effective, nontoxic delivery vehicles will need to be carried out to facilitate the broadest clinical application of RNAi.

2. Cell and Stem Cell Therapy

Cell therapy works by introducing new cells into a target tissue in order to treat a disease. These may be either cells from the patient (autologous) or cells from other patient, often a close relative (allogeneic). Occasionally, non-human cells may be used to produce a desired response in the patient (xenotransplantation) although this involves a new set of ethical considerations [19, 20, 21]. A large part of the research in this area is focusing on the use of stem cell therapies to treat, amongst others, cardiovascular disease, type-1 diabetes, and brain and spinal injuries.

3. Nanomedicine

The biological and medical research communities have exploited the unique properties of nanomaterials for various applications (e.g., contrast agents for cell imaging and therapeutics for treating cancer) [22, 23].

3.1. Targeted Drug Delivery System: Nanotechnology has been a boon for the medical field by delivering drugs to specific cells using nanoparticles [24]. The overall drug consumption and side effects can be lowered significantly by depositing the active agent in the morbid region only and in no higher dose than needed. An example can be found in dendrimers and nanoporous materials. Another example is to use block co-polymers, which form micelles for drug encapsulation. They could hold small drug molecules transporting them to the desired location. Another vision is based on small electromechanical systems; nanoelectromechanical systems are being investigated for the active release of drugs. Some potentially important applications include cancer treatment with iron nanoparticles or gold shells. A targeted or personalized medicine reduces the drug consumption and treatment expenses resulting in an overall societal benefit by reducing the costs to the public health system.

3.2. Implantable Delivery System: Nanotechnology is also opening up new opportunities in implantable delivery systems, which are often preferable to the use of injectable drugs, because the latter frequently display first-order kinetics (the blood concentration goes up rapidly, but drops exponentially over time) [25]. This rapid rise may cause difficulties with toxicity, and drug efficacy can diminish as the drug concentration falls below the targeted range. Other example is Buckyballs which can "interrupt" the allergy/immune response by preventing mast cells (which cause allergic response) from releasing histamine into the blood and tissues, by binding to free radicals "dramatically better than any anti-oxidant currently available, such as vitamin E [26].

3.3. Monoclonal Antibodies: Together with cancer biomarker advance, nanotechnology could lead to a "personalized oncology", where early tumour detection and diagnosis are more and more specific [27, 28]. A nanosized drug delivery system is mainly composed of three fundamental elements: i) a drug nanocarrier (1-100 nm), ii) an anti-cancer drug; iii) an active targeting molecule, recognizing a tumour associated marker expressed at the cell surface. These immunocomplexes are confirmed to be potentially used as targeted drug delivery system.

3.4. Tissue Engineering: Nanotechnology can help reproduce or repair damaged tissue. "Tissue engineering" makes use of artificially stimulated cell proliferation by using suitable nanomaterial-based scaffolds and growth factors. For example, bones can be regrown on carbon nanotube scaffolds. Tissue engineering might replace today's conventional treatments like organ transplants or artificial implants. Advanced forms of tissue engineering may lead to life extension [29, 30].

3.5. Targeting Gold Nanocages to Cancer Cells for Photothermal Destruction and Drug Delivery: The use of gold nanocages is a novel class of plasmonic nanoparticles, for photothermal applications. Gold nanocages are hollow, porous structures with compact sizes, precisely controlled plasmonic properties and surface chemistry [31, 32]. Release of the contents can be initiated remotely through near-infrared irradiation. Plasmonic nanoparticles provide a novel route to treat cancer due to their ability to effectively convert light into heat for photothermal destruction. Combined with the targeting mechanisms possible with nanoscale materials, this technique has the potential to enable highly targeted therapies to minimize undesirable side effects.

3.6. Nanorobots: Nanotechnology might be applied to dentistry as a new field called nanodentistry. Treatment possibilities might include the application of nanotechnology to local anesthesia, dentition renaturalization, the permanent cure for hypersensitivity, complete orthodontic realignment in a single visit, covalently bonded diamondized enamel, and continuous oral health maintenance using mechanical dentifrobots. Dental nanorobots could be constructed to destroy caries-causing bacteria or to repair tooth blemishes where decay has set in, by using a computer to direct these tiny workers in their tasks. Dental nanorobots might be also programmed to use specific motility mechanisms to crawl or swim through human tissue with navigational precision, to acquire energy, to sense and manipulate their surroundings, to achieve safe cytopenetration, and to use any of a multitude of techniques to monitor, interrupt, or alter nerve-impulse traffic in individual nerve cells in real time [33, 34, 35].

4. Biosimilars

Until recently, prescribers had to deal with generics, considered to be simple molecules that are easy to copy. But in fact, the biodisponibility of generics remains a source of uncertainty. Now there are biosimilars, limited for the time being in the cancer setting to granulocyte-colony stimulating factors (G-CSFs) and epoetins. Soon there will be biosimilar monoclonal antibodies with anticancer activity. Prescribers will ask, as they did for generics, if such drugs have the same activity as originators, if their safety profile is the same, if quality of the production process is guaranteed [36, 37]. Prescribers will want to know if their patients are indeed receiving the prescribed product, and not another. Finally prescribers will want to check that the lower cost of biosimilars will allow them to adhere to international guidelines. This should benefit patients and the community.

5. Transdermal Delivery Systems

5.1. Transdermal Delivery of Biopharmaceuticals: Transdermal delivery of biopharmaceuticals remains a hot topic in the pharmaceutical industry. Most players in this field are small but innovative companies [38, 39]. From a business point of view, products based on transdermal delivery of bioactive macromolecules have huge potential in many therapeutic areas, particularly in mass vaccination for influenza and HIV, as well as in managing diabetes. Currently, a variety of sophisticated transdermal delivery systems are in development pipelines. It is a daunting task to develop these devices into safe and efficacious products, let alone to mass-produce them at a reasonable cost.

5.2. TransPharma Drug Delivery System: TransPharma's ViaDerm drug delivery system incorporates a handheld electronic device, which creates microscopic passageways through the outer layer of the skin allowing for transdermal delivery of a wide variety of drugs from a patch. The system provides a cost-effective, easy-to-use, self-administered solution that enables the safe, reproducible and accurate delivery of a broad range of product candidates, including hydrophilic small molecules peptides and proteins. TransPharma Medical, a company developing transdermal drug delivery technology, has completed a Phase Ia trial of its ViaDerm-GLP1 agonist being developed to treat Type 2 diabetes [40].

6. Smart Medications and Drug Delivery Systems (SDDS): The ultimate goal of Smart Drug Delivery Systems (SDDS) is, to administer drugs at the right time, at the right dose anywhere in the body with specificity and efficiency which can help patients better adhere to their therapy regimen. SDDS can keep drugs at desirable levels in the body and avoid the need for frequent doses SDDS have specific characteristic features like pre-programmed, self regulated, control timed, targeted spatially, monitor drug delivery. SDDS include Magnetic Nanocapsules, microspheres, thermo-triggered squirting, Gold Nanocage that responds to light, micro and nano-electromechanical systems (MEMS or NEMS), nano beacon, various sensors like pressure or flow or electro-optical or glucose sensors. Nanotechnology based 'SMART' drug delivery systems are proved efficient in diagnosis and treatment of various diseases like hypertension and diabetes mellitus [41]. Use of Hydrogels, Nanomedicine and techniques like Microencapsulation are present in SMART drug delivery system. SDDS uses microchips/nanoparticles placed under the skin or into the spinal cord or brain that detects various chemical signals in the body to deliver drugs ranging from pain medication to chemotherapy. New therapy strategies, genetic diseases treatment, targeted and intelligent drug delivery, are health improvement techniques to the future generations.

6.1. Smart Medication Dispenser: The implementation of an automatic medication dispenser is required for users who take medications without close professional supervision [42, 43]. By relieving the user from the error-prone tasks of interpreting medication directions and administrating medications accordingly, the device can improve the rigor in compliance and prevent serious medication errors. By taking advantage of scheduling flexibility provided by medication directions, the device makes the user's medication schedule easy to adhere and tolerant to tardiness whenever possible. The medication scheduler and dispenser controller do this work collaboratively in an action-oriented manner. An advantage of this design is that new functions can be added and existing ones removed or revised with little or no need to modify the dispenser control structure.

6.2. Smart Medication Box "Control of Appliance Through Internet": The developments in network technologies provide opportunities to control appliances at homes and offices through the Internet [44]. If these technologies are used appropriately, they can contribute to the welfare of people in many aspects, such as health care. Considering the problems in health care industry and the problems that occur because of medicine noncompliance, we felt that there is a need for a medication dispenser system. By using Internet and home network technologies this system can aid controlling and monitoring patients who are on regular medication.

6.3. Smart Infusion Pumps: Smart infusion pumps have the potential to improve the safety of delivering medications. However, despite a cost of three to four times more than traditional pumps, achieving the safety benefits of smart pumps has been proven [45].

6.4. Smart Capsules: Triggered release systems based on physiological stimuli have emerged for advanced therapeutic delivery applications [46, 47]. Frank Caruso and co-workers combine several independent release mechanisms that synergistically function to tune cargo release profiles. The simple and efficient synthesis allows the design of "smart" capsules with dual stimuli responsive cargo release mechanisms for therapeutic applications.

6.5. SmartPill (A Prescription Drug Management System): Elderly, illiterate, uneducated, and otherwise impaired individuals have difficulty complying with prescription drug regimens. As a result, misuse is common among these types of patients. Researchers have documented a number of reasons for this problem, but the most common is confusion. SmartPill combats this problem in an innovative way

[48]. The product, which consists of an automated medication dispenser and special drug cartridges, reduces the risks associated with prescription drug use through the application of Information Technology (IT). As a result, SmartPill's approach is novel.

7. **Remotely Triggered Delivery Systems:** Systems that release drugs in response to a remote trigger, that is, systems that are actuated by an external stimulus, could offer distinct clinical advantages over those that release drugs passively or are triggered internally, e.g., by a chemical stimulus [49, 50]. Drug release profiles could be tailored to the specific therapy. For example, insulin is most effective when delivered to a diabetic in short bursts, whereas an anesthetic should be delivered in a steady, continuous fashion. Most importantly, perhaps, remotely triggered systems would allow the patient or physicians to control then dose, timing, and duration of drug release. Numerous stimuli could be used for drug triggering, including visible or near-infrared (NIR) light, electric or magnetic fields, and ultrasound. Some of these techniques, such as ultrasound, magnetic resonance imaging (MRI), and NIR fluorescence microscopy, are already used in the clinic or lab for imaging.

8. **Electronic Prescription:** Since physicians handwriting is really bad, it was only a matter of time before electronic prescriptions became popular [51]. By sending prescriptions in this way, it will become easier to see when prescriptions interact and when the patient is bringing in a valid prescription which will lead to prevention of medication errors and improving patients' healthcare [52, 53].

9. **Tell Us™: a Web-Based Tool for Improving Healthcare:** Routine electronic patient-reported outcome collection in patients with advanced disease could improve communication among patients, caregivers, and providers, the timeliness of identifying problems, and effectiveness of follow-up [54]. A Web-based tool aimed to collect symptoms and needed data and provide feedback to hospice and palliative care patients, caregivers, and providers. Tell Us™ based on an existing pure Web technology platform, the Medical Decision Logic, Inc., Health Science Process Framework. The software development process included eliciting information on systems and needs, mapping care processes with three diverse hospices, and soliciting ideas for the software from clinicians and researchers. A prototype software product, incorporated the hospices' processes, assessment questions, and educational materials, and refined the product with feedback from other hospice and palliative care professionals Tell Us™ includes modules for authoring and deploying clinical queries and completion schedules, for enrolling clinical sites and patients for patients and/or families to complete assigned assessments on a scheduled basis, and for providers to view patient-reported data. Tell Us™ provides customizable automated provider e-mail alerts based on patient responses (such as uncontrolled symptoms or need for medication refills) and provides educational materials targeted to patient needs. Future research will involve integrating the software into care and evaluating its feasibility and use for data collection, patient education, and improving outcomes.

10. **Smartphone For Improving Medication Adherence:** Medication nonadherence is a common, complex, and costly problem that contributes to poor treatment outcomes and consumes health care resources. Nonadherence is difficult to measure precisely, and interventions to mitigate it have been largely unsuccessful. Using smartphone adherence apps represents a novel approach to improving adherence. This readily available technology offers many features that can be designed to help patients and health care providers improve medication-taking behavior. Currently available apps were identified from the three main smartphone OSs (Apple, Android, and Blackberry). Adherence apps with advanced functionality were more prevalent on the Apple iPhone OS. Among all apps, MyMedSchedule, MyMeds, and RxmindMe rated the highest because of their basic medication reminder features coupled with their enhanced levels of functionality. Despite being untested, medication apps represent a possible strategy that pharmacists can recommend to nonadherent patients and incorporate into their practice [55].

11. **Radio Frequency Identification Technology (RFID):** RFID (Radio Frequency Identification) technology is expected to play a vital role in the healthcare arena, especially in times when cost containments are at the top of the priorities of healthcare management authorities. Medical equipment represents a significant share of yearly healthcare operational costs; hence, ensuring an effective and efficient management of such key assets is critical to promptly and reliably deliver a diversity of clinical services at the patient bedside. Empirical evidence from a phased-out RFID implementation in one European hospital demonstrates that RFID has the potential to transform asset management by improving inventory management, enhancing asset utilization, increasing staff productivity, improving care services, enhancing maintenance compliance, and increasing information visibility. Most importantly, RFID allows the emergence of intelligent asset

management processes, which is, undoubtedly, the most important benefit that could be derived from the RFID system. Results show that the added intelligence can be rather basic (auto-status change) or a bit more advanced (personalized automatic triggers). More importantly, adding intelligence improves planning and decision-making processes [56].

CONCLUSION

To meet with the needs of the new dynamic era of pharmaceutical research and health care environment, pharmaceutical education has to set new priorities to keep pace with the new discoveries.

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