# PHARMA FRONTLINE NEWS LETTER

Department of Pharmaceutics and Regulatory affairs

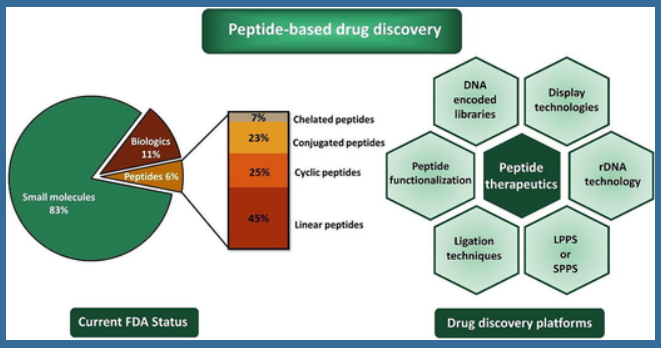
Faculty of Pharmacy
Sri Adichunchanagiri College of Pharmacy
B.G. Nagara - 571 448, Karnataka

ADICHUNCHANAGIRI UNIVERSITY

JULY- 2024 (BIMONTHLY) ISSUE # 7


## Dept. of Pharmaceutics & Regulatory Affairs

### PEPTIDE THERAPEUTICS: CURRENT STATUS AND FUTURE DIRECTIONS




- Traditional peptide technologies
- Peptide-based Drug discovery
- Peptides as therapeutics
- Peptide Drug market

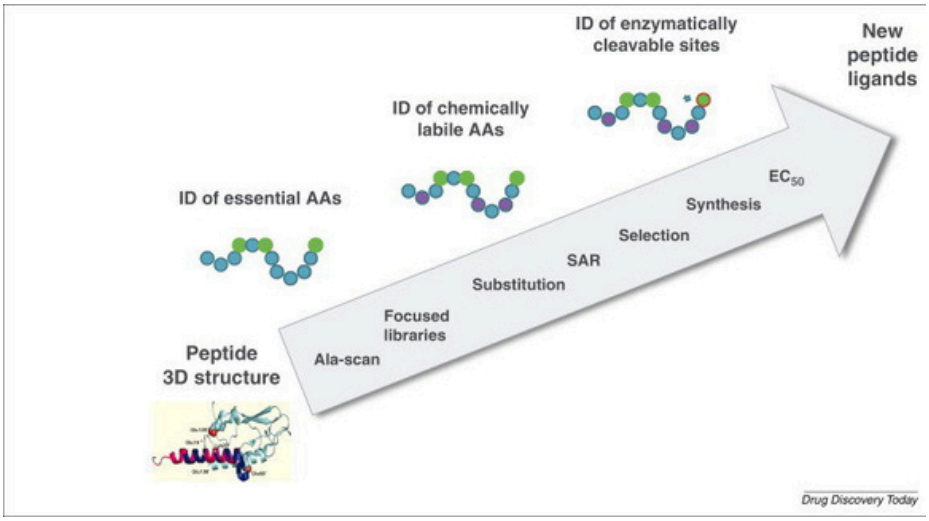
### CONTINUOUS MANUFACTURING

- History of Continuous Production
- Benefits
- Continuous Manufacturing Challenges
- Advantages of Continuous Manufacturing


### CURATIVE OR THERAPEUTIC CARE

- Gene therapy
- Genome editing
- Tissue engineering and cell therapy
- Blockbuster indications
- Regulatory action

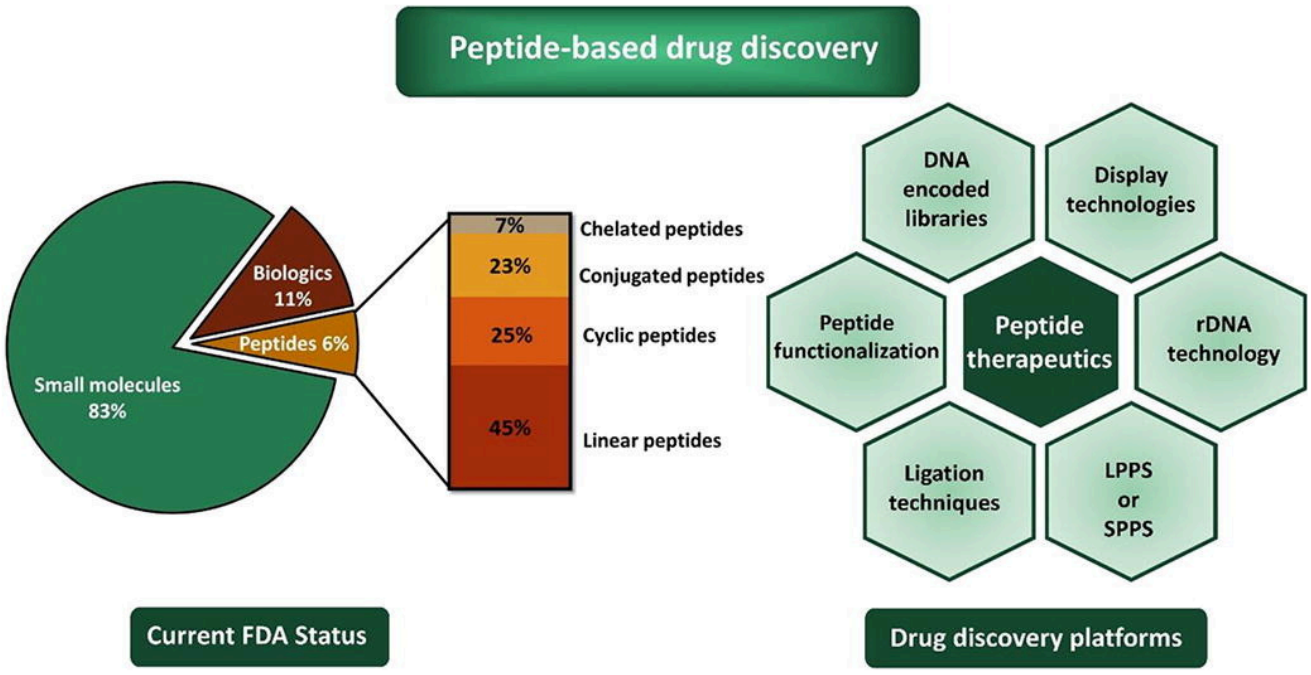
# PEPTIDE THERAPEUTICS:CURRENT STATUS AND FUTURE DIRECTIONS




**The traditional structure-based design strategies** that are used in peptide drug discovery. This includes substitution of amino acids (AA), and the building of structure–activity relations (SAR) via elements such as an alanine (Ala) scan and estimation of EC50 (half maximal effective concentration).

Peptides are recognized for being highly selective and efficacious and, at the same. time, relatively safe and well tolerated. Consequently, there is an increased interest in peptides in pharmaceutical research and development (R&D), and approximately 140 peptide therapeutics are currently being evaluated in clinical trials. Given that the low-hanging fruits in the form of obvious peptide targets have already been picked, it has now become necessary to explore new routes beyond traditional peptide design.

Examples of such approaches are multifunctional and cell penetrating peptides, as well as peptide drug conjugates. Here, we discuss the current status, strengths, and weaknesses of peptides as medicines and the emerging new opportunities in peptide drug design and development. More than 7000 naturally occurring peptides have been identified, and these often have crucial roles in human physiology, including actions as hormones, neurotransmitters, growth factors, ion channel ligands, or anti-infective. This aspect might also be the primary differentiating factor of peptides compared with traditional Small molecules. Furthermore, peptide therapeutics is typically associated with lower production complexity compared with protein-based biopharmaceuticals and, therefore, the production costs are also lower, generally approaching those of small molecules. Thus, in several ways, peptides are in the sweet spot between small molecules and biopharmaceuticals. Naturally occurring peptides are often not directly suitable for use as convenient therapeutics because they have intrinsic weaknesses, including poor chemical and physical stability, and a short circulating plasma half-life. These aspects must be addressed for their use as medicines. Some of these weaknesses have been successfully resolved through what we term the 'traditional design' of therapeutic peptides.




## Peptides as therapeutics

The importance of small molecules as drugs in the management of diseases is undeniable. At the same time, detailed pathological insights and side effects associated with small-sized drugs have created a need for alternative therapeutic prepositions. Peptides represent a distinct class with some properties of small-sized drugs as well as attributes of large proteins and other biologics [1]. Most intrinsic signaling entities, such as enzymes, hormones, and immune response mediators

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## PEPTIDE DRUG MARKET

DURING THE PAST DECADE, PEPTIDES HAVE GAINED A WIDE RANGE OF APPLICATIONS IN MEDICINE AND BIOTECHNOLOGY, AND THERAPEUTIC PEPTIDE RESEARCH IS ALSO CURRENTLY EXPERIENCING A RENAISSANCE FOR COMMERCIAL REASONS. FOR EXAMPLE, THE PEPTIDE-BASED MEDICINE LUPRONTM FROM ABBOTT LABORATORIES FOR THE TREATMENT OF PROSTATE CANCER AND MORE, ACHIEVED GLOBAL SALES OF MORE THAN US$2.3 BILLION IN 2011 IN ADDITION, LANTUSTM FROM SANOFI (WHICH IS REALLY AT THE BORDER BETWEEN A PEPTIDE DRUG AND A SMALL BIOPHARMACEUTICAL) REACHED SALES OF US$7.9 BILLION IN 2013

# CONTINUOUS MANUFACTURING

Continuous manufacturing is a method for manufacturing pharmaceutical products from end-to-end on a single, uninterrupted production line.
Where batch manufacturing requires transporting, testing, and re-feeding materials from one process to the next, continuous processes execute all testing, feeding, and processing inline. Sophisticated process analytical technologies ensure quality in-process.

## BENEFITS

Continuous manufacturing helps firms eliminate hold times, utilize the full capacity of their manufacturing lines, and bring quality testing inline.
Continuous manufacturing can also help manufacturers react more quickly to changes in demand. A continuous line can process higher and lower quantities of a drug as needed, it allows manufacturers to respond more rapidly to changing markets. It also enables recipes not possible using traditional batch methods.
In short, the benefits of continuous manufacturing are:

- Improved utilization
- Flexible batch sizes
- Simplified scaling
- Greater control over critical process parameters
- Less energy consumption
- Better adherence to schedules

## History of Continuous Production

Though new to pharmaceutical manufacturing, continuous manufacturing isn't new.
In fact, continuous processes have been the norm in some industries for nearly a century. Continuous production has a long history in iron production, where facilities can run uninterrupted for years. It's also the norm in the petrochemical industry, as well as some food and beverage processes.
Here are examples of continuous manufacturing industries and products:

- Oil Refining
- Metal smelting
- Paper
- Pastes
- Some foods and beverages, like peanut butter

The turn to continuous manufacturing in the pharmaceutical industry has gained momentum over the last decade. Manufacturing technology matured enough to accommodate the complex manufacturing techniques used in pharmaceutical production. Sensors and analytical technology matured enough to bring quality control in-line. And the regulatory and economic environment encouraged manufacturers to pursue innovation. The FDA quickly recognized the potential of continuous manufacturing to improve quality, meet demand, and improve service to patients, and they've consistently voiced their support.

# CONTINUOUS MANUFACTURING CHALLENGES

**Manual Changeovers**

For one, changeovers on continuous manufacturing lines are complicated and can take over a week to perform. Continuous manufacturing systems have thousands of parts that need to be cleaned, changed out, and verified. Changeovers are a highly manual process (one made easier by digital SOPs), and they can be time-consuming for even skilled operators.

As one expert put it:

“Whether frequent changeovers can be performed efficiently to enable short duration runs and small batches is still an open question. While the desired goal is to be able to changeover in less than a day, current lines can take a week or more for changeover due to the extensive time for disassembling, cleaning, and reassembling.”

**Difficult Training**

Operating continuous manufacturing equipment requires extensive training. The complexity of the equipment and the risk of mistakes means that everyone involved needs sufficient exposure and understanding of the system to ensure proper usage.

**Complex Economics**

While there are clear manufacturing benefits to continuous manufacturing systems, the economics of the pharmaceutical industry has presented a challenge. Between expenditures for new equipment, abandoning existing capacity, and projections for lifetime profitability of a given therapy, manufacturers are always concerned with the returns on any investment in continuous manufacturing technology.

## ADVANTAGES OF CONTINUOUS MANUFACTURING

THE BENEFITS OF CONTINUOUS MANUFACTURING INCLUDE:

- REDUCED MANUFACTURING COSTS, PARTICULARLY OVER THE LONG TERM
- SHORTER PRODUCTION TIMES – REDUCING MANUFACTURING TIMES FROM WEEKS TO DAYS IS NOT UNUSUAL
- REDUCES THE RISK OF HUMAN ERROR
- IMPROVES QUALITY
- MONITORING IS MORE EFFICIENT AS CONTINUOUS MANUFACTURING PROCESSES TYPICALLY USE AUTOMATED MONITORING TECHNIQUES AND PREDICTIVE MAINTENANCE

# CURATIVE OR THERAPEUTIC CARE


**Curative or therapeutic care refers** in part to treatments and therapies provided to a patient with the goal of curing an illness or condition. The terms are also used for treatments that delay disease progression even when a cure is not possible. It is important to understand the risks and benefits of any curative or therapeutic care so you can make the best choices for you and your life. Shared decision making can help you with that understanding

**Examples of curative care include:**

- Antibiotics for bacterial infections
- Chemotherapy or radiation therapy for cancer
- Cast for a broken bone
- Dialysis treatment for kidney failure
- Surgery for appendicitis
- Acupuncture for certain conditions
- Dietary programs for certain conditions

## Gene therapy

Pfizer has taken steps to enter the gene therapy field by appointing Michael Linden, a gene therapy expert, to a 2-year secondment within Pfizer's Rare Disease Unit. The company has also made an agreement with Spark Therapeutics to develop SPK-FIX, a bio-engineered adeno-associated virus (AAV) vector for the treatment of hemophilia B. Phase 1/2 clinical trials were expected to start in the first half of 2015.

Pfizer will be responsible for any pivotal studies and regulatory submissions. Spark Therapeutics could receive double-digit royalties on the basis of global product sales.

The Sanofi subsidiary Genzyme and the Cambridge (MA)-based gene therapy startup Voyager Therapeutics announced a broad collaboration for a range of neurobiological diseases.

GlaxoSmithKline (GSK) plans to file an application for approval of its own adenosine deaminase–severe combined immunodeficiency (ADA-SCID) program by the European Medicines Agency (EMA) in the next few months and is in active discussions with the US Food and Drug Administration (FDA) for filing in the United States.

## Genome editing

**Genome editing uses DNA nucleases or 'molecular scissors' to create specific breaks in genes and allows the endogenous repair mechanisms of the cell, together with an introduced corrective template, to repair the induced break (Top image). The families of nucleases include zinc finger nucleases, transcription activator–like effector nucleases, mega nucleases and the CRISPR-Cas9 system.**

**Clinically, the most advanced in the genome editing space is Sangamo BioSciences, which uses zinc finger technology for genome editing**

**The company's lead program in HIV is an autologous zinc finger–modified T cell product that is currently in phase 2 trials in HIV-infected subjects. It works by introducing a mutation into CCR5, the T cell surface receptor that is used by HIV-1 for cell entry.**

## Tissue engineering and cell therapy

In the past few years, regenerative medicine and advanced technologies has become a dynamic and rapidly changing field, owing to numerous positive clinical trial results. Many new companies have emerged, and programs are moving from academia to the corporate world.

Regenerative medicine includes the tissue engineering and cell-therapy space. Products may be scaffold or matrix material alone, cells or a combination of both used to create the desired effect and therapeutic model. Cells may be autologous (patient derived) or allogeneic (donor derived). Cardiology, orthopedics, skin and wound healing, diabetes and central nervous system disorders continue to be the commercial markets for products.

TiGenix's ChondroCelect, a cell-based product for cartilage repair in the knee, has been approved in Europe. The company has other products in the pipeline for Crohn's disease, rheumatoid arthritis, sepsis and autoimmune disease

## Blockbuster indications

Traditionally, gene therapy has been associated with the treatment of rare genetic diseases; however, it has the potential to treat a broader array of indications, such as HIV, retinal diseases, hemophilia, heart failure and cancer.
Early successes with gene therapy for these indications show that it could compete with and even disrupt current treatments.

## REGULATORY ACTION

**Regenerative medicine presents a regulatory challenge because a product may be considered a biologic, a medical device or a combination of the two. The FDA's Office of Combination Products determines the primary method of action and therefore the appropriate regulatory pathway.**

**Although a company's reimbursement and regulatory strategies will preferably be aligned, it is possible to have a product regulated as a medical device and reimbursed as a cell therapy within one country and multiple reimbursement categories from each country in which the product is sold**

**Gene therapy typically targets extremely rare orphan diseases, so clinical trials are necessarily small and might not use a control group or blinding procedures before phase 3 trials. EMA can grant marketing authorization under 'exceptional circumstances', recognizing the potential benefit of a product in light of incomplete information about a disease (typically owing to the small patient population) as well as the risks associated with the therapy.**

Ophthalmic disease and hemophilia are indications that feature prominently in gene therapy indications. Eye diseases are well understood and are often caused by a single gene mutation, and there are good predictive animal models that enable rapid clinical testing. In this field, the FDA consistently applies four accepted endpoints–visual acuity, visual fields, contrast sensitivity and color vision and provides guidance on how much improvement is required for a therapy to be considered clinically relevant. Clearly defined endpoints help accelerate the approval process.

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# New Drug Approvals

- Pyzchiva (ustekinumab-ttwe) Injection
  Date of Approval: June 28, 2024
  Company: Samsung Bioepis Co., Ltd.
  Treatment for: Plaque Psoriasis, Psoriatic Arthritis, Crohn's Disease, Ulcerative Colitis

- Vigafyde (vigabatrin) Oral Solution
  Date of Approval: June 17, 2024
  Company: Pyros Pharmaceuticals, Inc.
  Treatment for: Infantile Spasms

- Erzofr (paliperidone palmitate) Extended-Release Injectable Suspension
  Date of Approval: July 26, 2024
  Company: Luye Pharma Group
  Treatment for: Schizophrenia, Schizoaffective Disorder

- Zunveyl (benzgalantamine) Delayed-Release Tablets - formerly ALPHA-1062
  Date of Approval: July 26, 2024
  Company: Alpha Cognition Inc.
  Treatment for: Alzheimer's Disease

- Leqselvi (deuruxolitinib phosphate) Tablets
  Date of Approval: July 25, 2024
  Company: Sun Pharmaceutical Industries Inc.
  Treatment for: Alopecia Areata

- Kisunla (donanemab-azbt) Injection
  Date of Approval: July 2, 2024
  Company: Eli Lilly and Company
  Treatment for: Alzheimer's Disease

- Iqirvo (elafibranor) Tablets
  Date of Approval: June 10, 2024
  Company: Ipsen Biopharmaceuticals, Inc.
  Treatment for: Primary Biliary Cholangitis

- Rytelo (imetelstat) for Injection
  Date of Approval: June 13, 2024
  Company: Grifols USA, LLC
  Treatment for: Primary Immunodeficiency Syndrome

# DEPARTMENT ACTIVITIES

## Publications in Scopus Indexed/Web of Science Journals


# Research on Alzheimer's Disease (AD) Involving the Use of In vivo and In vitro Models and Mechanisms

Sweta Sinha [1], Pranay Wal [2], Prakash Goudanavar [3], Surisetti Divya [4], Vishwadeepak Kimothi [5], Divya Jyothi [6], Mukesh Chandra Sharma [7], Ankita Wal [2]

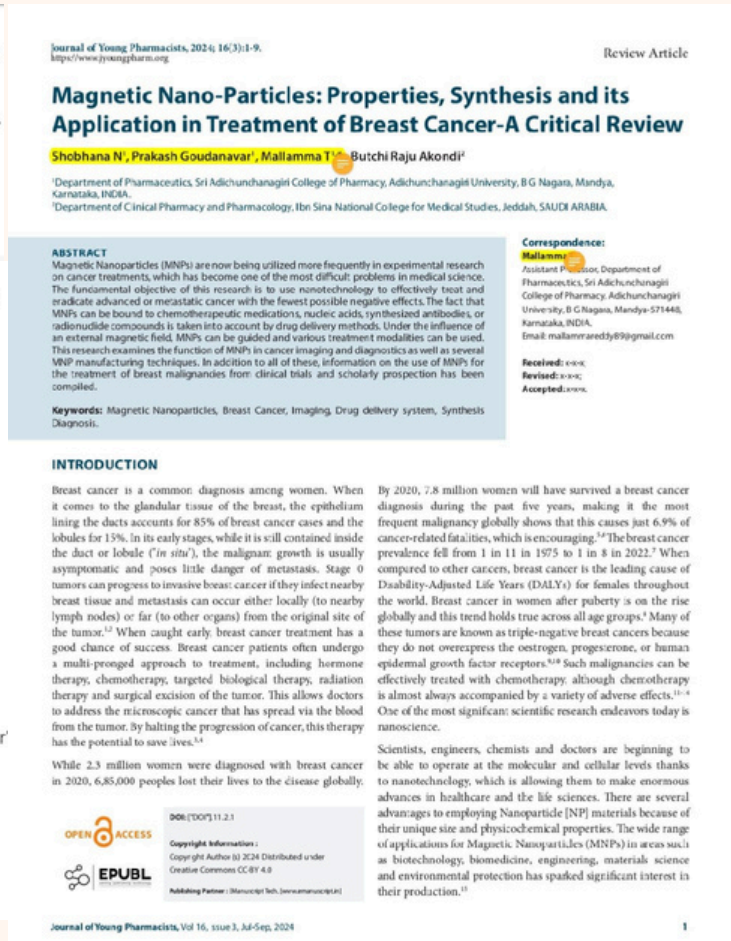
Affiliations + expand

PMID: 38803173 DOI: 10.2174/0118715249293642240522054929

## Abstract

**Background:** Alzheimer's Disease (AD) is a neurodegenerative disorder characterized by the progressive formation of extracellular amyloid plaques, intracellular neurofibrillary tangles, inflammation, and impaired antioxidant systems. Early detection and intervention are vital for managing AD effectively.

**Objective:** This review scrutinizes both in-vivo and in-vitro screening models employed in Alzheimer' disease research. In-vivo models, including transgenic mice expressing AD-related mutations, offer profound insights into disease progression and potential therapeutic targets. A thorough understanding of these models and mechanisms will facilitate the development of novel therapies and interventions for Alzheimer's disease. This review aims to provide an overview of the current experimental models in AD research, assess their strengths and weaknesses as model systems, and underscore the future prospects of experimental AD modeling.





# DEPARTMENT ACTIVITIES

## Publications in Scopus Indexed/Web of Science Journals

https://doi.org/10.33472/AFJBS.6.8.2024.141-153

AFJBS African Journal of Biological Sciences

Research Paper Open Access

### INVESTIGATION OF THE STRUCTURAL AND FUNCTIONAL PROPERTIES OF STARCH-G-POLY (ACRYLIC ACID) HYDROGELS REINFORCED WITH CELLULOSE NANOFIBERS FOR CU2+ ION ADSORPTION

**Ankita Tripathi[1], Nakul Gupta[2], Bharti Chauhan[3], Neha Priya[4], Prakash S. Sukhramani[5], Harshad Jitubhai Trivedi[6], Mallamma T[7], Vidyashree N H[8], Rajesh Dodiya*[9], Keshamma E[10], Suraj Mandal[11]**

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## Textbook of INDUSTRIAL PHARMACY

**Volume - 3**

### Chapter - 3

### Pharmaceutical Aerosols

**Mallamma T**

**Abstract**

Pharmaceutical aerosols are a crucial dosage form that must be considered alongside other forms such as tablets, capsules, and solutions. Due to their widespread use, high patient and physician acceptance, and prevalence in the market, they have become a vital option for delivering medications to the lungs and nasal passages for conditions like asthma, chronic obstructive pulmonary disease (COPD), and allergic rhinitis. They represent a sophisticated form of medication that allows for the targeted


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Micro and Nanosystems, xxxx, xx, x-x 1

REVIEW ARTICLE

### Drug Delivery and Monitoring through Wearable Devices with Microneedles in the Field of the Health Care System

Kumarswamy K.C.[1,*], Madhu B.K.[1], N. Raghavendra Naveen[1], Prakash S. Goudanavar[1] and Purushotham K.N.[2]

[1]*Department of Pharmaceutics, Sri Adichunchanagiri College of Pharmacy, Adichunchanagiri University, BG Nagara, Karnataka, 571448, India;* [2]*Department of Pharmaceutical Chemistry, Sri Adichunchanagiri College of Pharmacy, Adichunchanagiri University, BG Nagara, Karnataka, 571448, India*

ARTICLE HISTORY

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DOI:
10.2174/0118764029311292240603050113

**Abstract:** Microneedles represent a revolutionary advancement in drug delivery and diagnostics, offering a minimally invasive approach to accessing the intricate biological environment of the human body. These micron-sized needles, typically ranging from 25 to 1000 micrometers in length, penetrate the outermost layer of the skin, creating microchannels that facilitate the transdermal administration of therapeutics or the extraction of interstitial fluid for analysis. This innovative technology holds great promise for enhancing patient compliance, reducing side effects, and improving the overall efficiency of drug delivery. Integrating microneedles with wearable devices further amplifies their potential impact. Wearable devices provide a seamless interface for monitoring and controlling microneedle-based systems, fostering real-time data collection and personalized healthcare. Such devices can be designed to administer precise drug doses at predetermined intervals, adapting treatment regimens to individual patient needs.

Additionally, the combination of microneedles and wearable devices enables continuous monitoring of biomarkers through the extraction of interstitial fluid, offering a non-invasive method for disease diagnosis and management. The review also provides a detailed overview of the mechanisms, types, fabrication techniques, applications, and patents for integrating microneedles with wearable devices. This symbiotic relationship between microneedles and wearables opens new paths for patient-centric healthcare, with the potential to transform chronic disease management and streamline therapeutic interventions. As these technologies continue to evolve, their integration may pave the way for personalized, on-demand healthcare solutions, accompanying a new era of patient well-being and treatment efficacy.

**Keywords:** Wearable devices, non-invasive, integrating microneedles, chronic disease, therapeutic intervention, delivery patches.

#### 1. INTRODUCTION

Insufficient enzymatic breakdown or drug absorption are the challenges in the GI tract or liver, so using an uncomfortable hypodermic needle for injections becomes the standard substitute. Alternatively, a more patient-friendly approach, providing the potential for controlled release over an extended period, involves administering the drug through a skin patch [1, 2]

To overcome the substantial challenge posed by the stratum corneum, which is the outermost layer of the skin layer and greatly restricts the transdermal delivery of most drugs at therapeutic rates, several approaches have been explored. These encompass the examination of lipid and chemical enhancers, among other approaches, to enhance skin permeability [3, 4] by using electroporation and iontophoresis techniques [5, 6] using optoacoustic or ultrasonic events force applied by the oscillations [7, 8]. All of these methods seek to alter the structural integrity of the stratum corneum, creating "openings" of nanometer dimensions through which molecules can traverse. The size of these disruptions is thought to be sufficiently small to facilitate the passage of small drugs and, in certain instances, macromolecules. Importantly, they are likely small enough to avoid causing clinically significant damage.

# DEPARTMENT ACTIVITIES

## ATTENDED ONE DAY SYMPOSIUM

Organized by Centre of excellence in Regulatory Sciences (CEReS) Department of pharmaceutics, on **“GMP Compliances and export/import opportunities - Regulator’s view”** to the Academics, Industry, Regulatory personnel on **6th April 2024**, from the eminent Speakers - **Dr D ROY, Ex Deputy Drugs Controller (India), CDSCO. Dr JAGASHETTY, Ex Drugs Controller, Karnataka. Dr A RAMKISHAN, Deputy Drugs Controller (India)**, at **JSS College of pharmacy**, Sri Shivarathreeshwara nagara, Mysuru-570015.



Department of Pharmaceutics and Regulatory Affairs, Organized One Day Seminar on “REGULATORY AFFAIRS TODAY: ENHANCING COLLABORATION BETWEEN INDUSTRY AND ACADEMIA” on 8th June 2024

Speakers – Mr. Selvakumar Subramanian, Deputy General Manager, Regulatory Affairs, Strides Pharma Science Limited, Bengaluru, India and Mr. Shanmuga Sundaram V, Group leader, Regulatory Affairs, Strides Pharma Science Limited, Bengaluru.

On **15th July 2024**, a Cultural program felicitation ceremony was held at the AIMS to honour participants who contributed to the **cultural performances** during the recent **National Assessment and Accreditation Council (NAAC) team visit**. The highlight of the event. The chief guest, **Vice Chancellor - Dr. M A Shekar**, along with **Registrar - Dr. C K Subbaraya** & **AIMS Principal & Dean - Dr. M G Shivaramu** , handed over the awards. **Vote of appreciation :** For the Participants who are involved in the cultural events given by **Our beloved Principal & Dean - Dr Bharthi D R**