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Bio wearable Drug Delivery Systems (BW-DDS): A Review

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Abstract:
The biowearable industry often tests skin devices on animals or humans, which can be difficult and unethical. We created a skin phantom kit that mimics skin's structure, sweat, and electrical properties, allowing students to study how these factors affect measurements using simple tools. A comsol simulation was also developed to analyze skin properties, electrode placement, and sweat effects, helping scale the model to realistic sizes. We also explored hydrogel nanocomposites for better biomedical applications and hormonal bioinspired models for AI and neurorehabilitation. Finally, we designed a wearable EMG prototype to monitor wrist activity for Carpal Tunnel Syndrome, highlighting the potential of wearable health technology while emphasizing data privacy and safety.

Keywords: Biomaterials, polyurethane, regenerative medicine, tissue engineering, tissue repair.

Introduction:
Biowearable drug delivery systems (DDS) are devices that can deliver drugs directly to the body over time while being worn, like patches, tattoos, or smart sensors.They combine biomedical engineering, electronics, and pharmacology to make drug administration more precise and personalized. BioWearable Drug Delivery Systems (BW-DDS) are modern devices designed to deliver medicines directly to the body in a controlled and precise way. Unlike traditional methods like pills or injections, these wearable systems can release drugs continuously or on-demand, making treatment more effective and patient-friendly.[1,3]

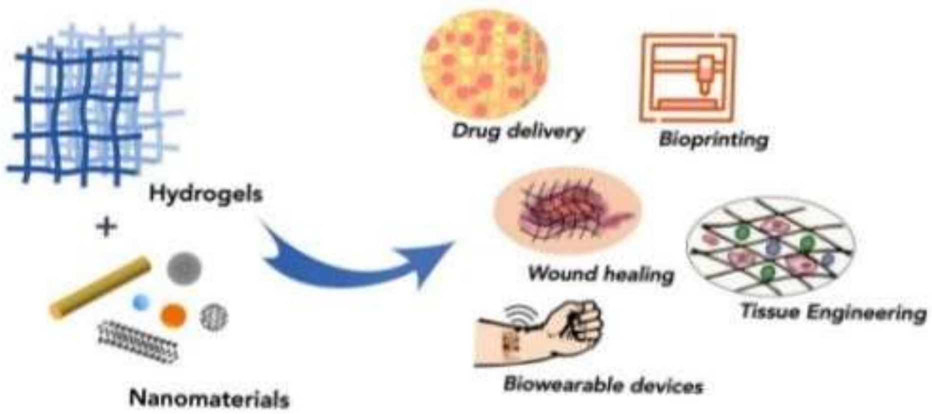

Fig 1: Schematic showing the broad applicability of hydrogel nanocomposites in the biomedical industry

Importance in Modern Healthcare:
BW-DDS improves patient care by increasing adherence, reducing side effects, and allowing personalized therapy. Many devices can monitor health in real-time, adjust drug doses automatically, and even share data with healthcare providers, making treatment safer and more efficient.

Evolution from Traditional to Smart/Wearable Systems:
Biowearable Drug Delivery Systems (BW-DDS) are modern devices designed to deliver medicines directly to the body in a controlled and precise way. Unlike traditional methods like pills or injections, these wearable systems can release drugs continuously or on-demand, making treatment more effective and patient-friendly.[2]

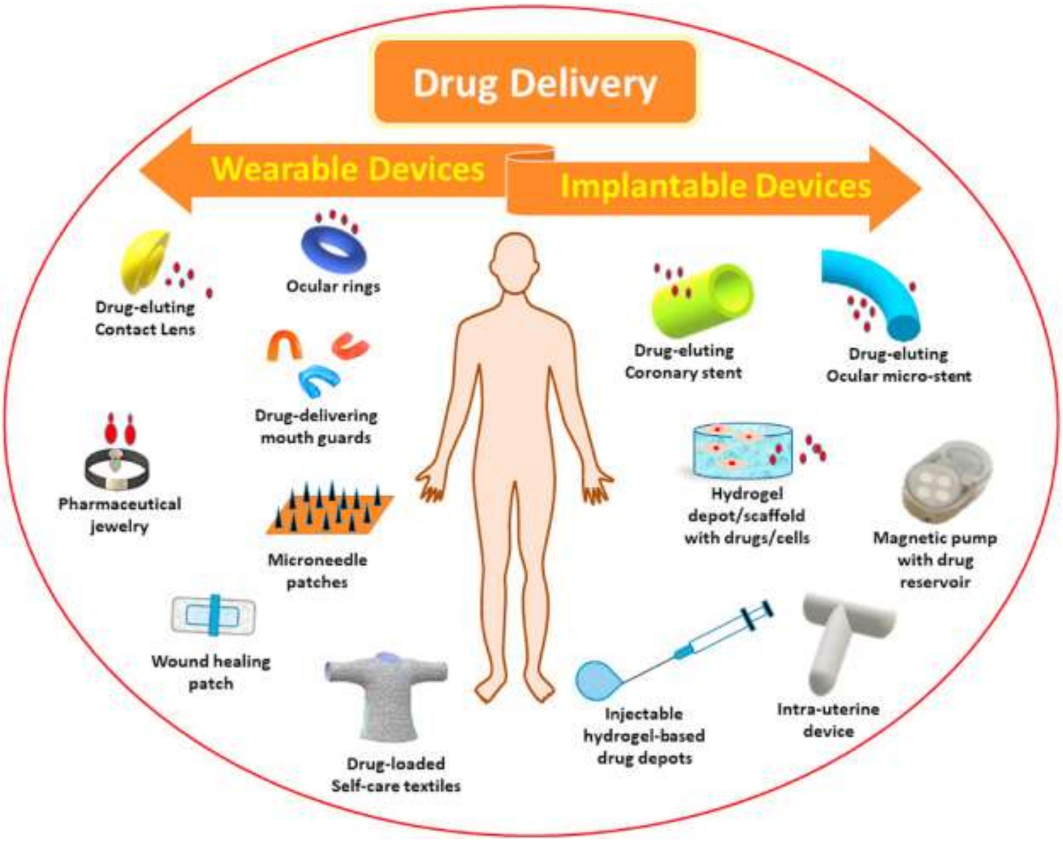

Fig 2: Wearable and implantable devices for drug delivery

Principal / working mechanism:
1. **Basic Concept of Controlled & Continuous Drug Delivery:** Drugs are released at a precise rate over a long period. Maintains therapeutic drug levels, avoiding peaks and troughs. Can be on-demand or automatic, depending on patient condition.
2. **Interaction between Device and Human Body:** Device monitors biomarkers like glucose, heart rate, or sweat composition. Detects body signals and adjusts drug release according .Ensures personalized and safe therapy.[3]

Mechanism of Drug Release:
- **Diffusion:** Drug slowly passes through a membrane or hydrogel.

- **Osmosis:** Drug is pushed out by water absorption.
- **Micro needles:** Painless penetration into skin for controlled release. Electrochemical / Stimuli-responsive: Release triggered by pH, temperature, or electrical signals.[4]

Integration of Sensors, Pumps, and Electronics:
- **Sensors:** Measure physiological parameters.
- **Micro-pumps:** Control the precise flow of drug. Electronics & Software: Process data and regulate drug release in real-time
- **Connectivity:** Some devices transmit data to healthcare providers.

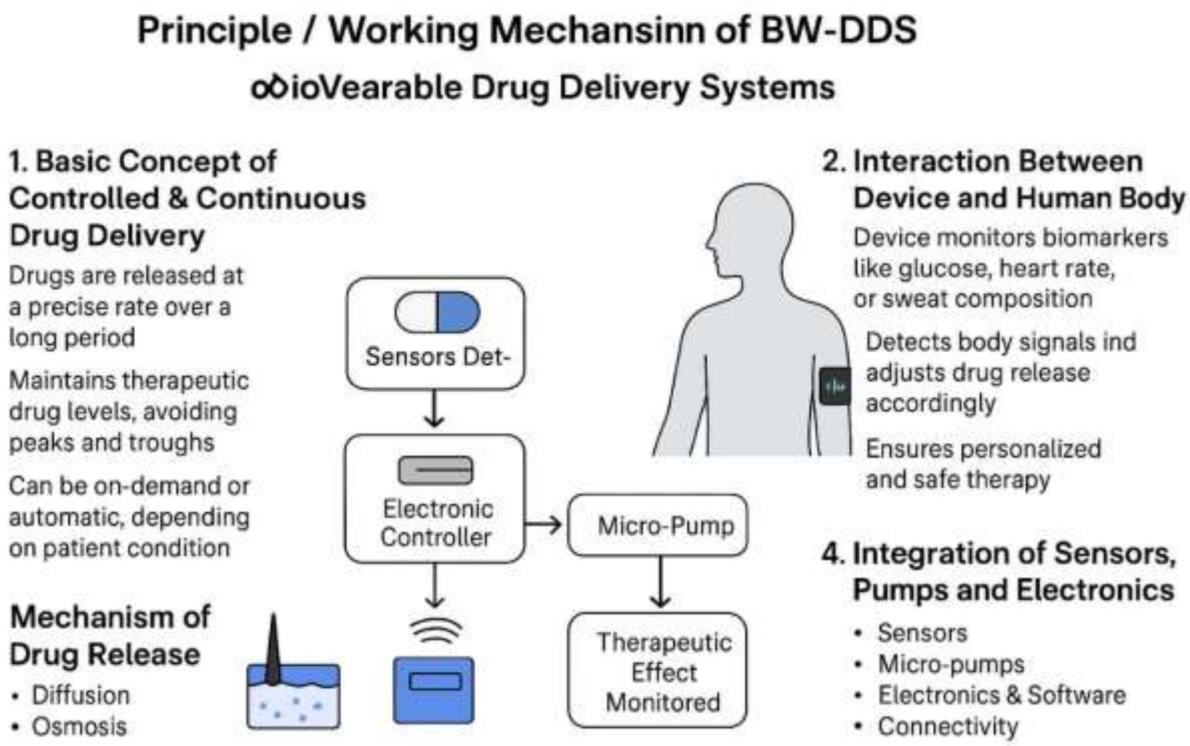

Fig 2: Working mechanism of BW-DDS

Types of BioWearable Drug Delivery Systems:

1. Transdermal Patches:

Adhesive systems applied to skin for controlled, sustained drug release.Widely used for pain management, hormone therapy, and nicotine replacement.
- **Advantages:** Non-invasive, improved patient adherence, consistent plasma drug levels.
- **Limitations:** Restricted to drugs with suitable skin permeability; risk of local irritation.

2. Micro needle-Based Systems:

Arrays of micro-needles penetrate the skin painlessly to delivece drugs.Capable of administering macromolecules such as insulin and vaccines.
- **Advantages:** Minimally invasive, avoids first-pass metabolism.
- **Limitations:** Limited drug loading, relatively higher production costs.[4]

3. Wearable Smart Injectors / Pumps:

Devices programmed to deliver precise doses automatically.Often integrated with sensors to respond to real-time physiological signals.

- **Applications:** Diabetes (insulin), chemotherapy, hormone therapies.
- **Advantages:** Personalized dosing, continuous therapy, improved therapeutic control.
- **Limitations:** Device cost, maintenance requirements, battery dependence.

4. Electrochemical / Iontophoretic Systems:

Utilize low electrical currents to drive ionic or charged drugs across the skin.Can be combined with sensors for feedback-controlled delivery.

- **Advantages:** Non-invasive, controllable rate, suitable for localized delivery.
- **Limitations:** Restricted to ionizable drugs; possible skin irritation.

5. Hydrogel-Based Wearables:

Hydrophilic polymer matrices that release drugs in response to stimuli (pH, temperature, glucose).Common in wound healing and localized drug therapy.

- **Advantages:** Biocompatible, sustained and stimuli-responsive drug release.
- **Limitations:** Mechanical weakness, mainly suitable for localized applications.

6. Smart Fabrics / Textiles:

Incorporate drugs or nanoparticles within clothing or fabric for continuous delivery.Potential applications include chronic disease management and sports recovery.

- **Advantages:** Comfortable, continuous, and discreet drug administration.
- **Limitations:** Experimental stage, limited drug loading capacity.[5]

Materials Used in BioWearable Drug Delivery Systems:

BioWearable drug delivery systems (BW-DDS) are advanced therapeutic devices designed to administer drugs in a controlled, continuous, and patient-friendly manner. The choice of materials is crucial to ensure biocompatibility, flexibility, mechanical durability, drug stability, and integration with electronics. The materials used in BW-DDS can be classified into five major categories:

1. **Polymers:**

Polymers form the structural and functional backbone of wearable drug delivery systems. They are versatile and can be engineered to control drug release, mechanical properties, and biodegradability.

- **Natural Polymers:** Chitosan, alginate, gelatin, hyaluronic acid, and cellulose derivatives.
- **Advantages:** Biocompatible, biodegradable, low toxicity, good for skin contact.
- **Applications:** Microneedle arrays, hydrogel matrices, and transdermal patches.
- **Synthetic Polymers:** Poly(lactic-co-glycolic acid) (PLGA), polyethylene glycol (PEG), polyvinyl alcohol (PVA), polycaprolactone (PCL).
- **Advantages:** Controlled degradation rates, tunable mechanical strength, precise drug release profiles.
- **Applications:** Long-term patches, implantable drug delivery devices, structural support for electronics integration.Smart/Stimuli-Responsive Polymers : PNIPAM, PAA, and other polymers responsive to temperature, pH, or biochemical signals.
- **Function:** Enable on-demand drug release based on physiological cues.[6]

Hydrogels and Silicon Materials:

These materials provide soft, flexible, and biocompatible interfaces with the skin and body tissues.

- **Hydrogels:** Three-dimensional, water-swollen polymer networks (e.g., polyacrylamide, gelatin, PVA).
- **Properties:** High water content, biocompatibility, tissue-like elasticity, and permeability.
- **Applications:** Microneedle bases, transdermal drug reservoirs, controlled release matrices.

Silicon Materials (Elastomers):

- Polydimethylsiloxane (PDMS) and silicone-based elastomers are commonly used.
- **Properties:** Flexibility, stretchability, skin conformability, chemical stability, and durability.
- **Applications:** Device encapsulation, flexible microfluidic channels, and wearable patch substrates.

Electronic Components:

- Electronics enable intelligent, responsive, and personalized drug delivery in BW-DDS.
- **Sensors:** Biosensors (glucose, lactate, hormones) and physical sensors (temperature, heart rate, strain) for real-time monitoring
- **Microcontrollers (MCUs) and ICs:** Process data, control drug release, and communicate with external devices.
- **Actuators:** Micro-pumps, valves, and electrochemical or thermal triggers for controlled drug administration.
- **Power Sources:** Rechargeable batteries, thin-film batteries, and energy-harvesting devices.
- **Communication Modules:** Bluetooth, NFC, or Wi-Fi for remote monitoring and data transfer.
- **Flexible Electronics:** Stretchable conductive traces, conductive polymers, and miniaturized circuits integrated into wearable matrices.
- **Importance:** Electronics transform conventional drug delivery into data-driven, feedback-controlled, and personalized therapy. .[7]

Adhesive materials:

- Adhesives ensure that bio-wearable devices stay securely attached to the skin without causing irritation.Medical-Grade Adhesives: Silicone-based, acrylic, or hydrocolloid adhesives.
- **Properties:** Strong yet skin-friendly, non-toxic, breathable, and flexible.
- **Applications:** Transdermal patches, wearable sensors, and microneedle arrays.
- **Importance:** Maintains device stability, drug absorption, and patient comfort during long-term use.
- **Protective Coatings:**Protective coatings safeguard both the device and the patient.
- **Purpose:**Protects sensitive electronics from moisture and sweat.Prevents drug degradation due to environmental exposure.Reduces skin irritation and allergic reactions.
- **Materials:** Thin polymeric layers, parylene coatings, silicone, or biocompatible hydrophobic layers.
- **Applications:** Coatings over microneedles, electronic circuits, and drug reservoirs to ensure long-term device reliability and safety.[8]

Key Considerations for Material Selection:

- **Biocompatibility:** Avoids immune reactions, irritation, or cytotoxicity.
- **Mechanical Properties:** Provides flexibility, stretch ability, and durability.
- **Drug Compatibility:** Maintains drug stability and release kinetics.
- **Integration Capability:** Ensures seamless incorporation of electronics, sensors, and actuators.
- **Patient Comfort:** Contributes to long-term adherence and usability.

Components and Design Aspects in BioWearable Drug Delivery Systems:

BioWearable drug delivery systems are advanced therapeutic devices that combine drug reservoirs, electronics, sensors, and flexible materials to enable controlled, continuous, and personalized drug administration. The design of these systems requires careful consideration of component selection, device architecture, and integration for patient comfort and efficacy.

Key Components of BW-DDS:

- **Drug reservoirs:** Store the therapeutic agent in liquid, gel, or solid form.
- **Materials used:** polymers, hydrogels, or microcapsules.
- **Delivery Mechanisms:** Micro needles: Pain-free penetration of the skin for transdermal delivery.
- **Micro-pumps:** Electrically or mechanically controlled to release precise drug doses.
- **Diffusion membranes:** Control the rate of drug release from the reservoir.
- **Sensors:** Monitor physiological parameters (glucose, pH, temperature, heart rate).Enable feedback-controlled or responsive drug release.
- **Electronics:** Microcontrollers (MCUs): Process sensor data and control actuators.
- **Communication modules:** Bluetooth, NFC, or Wi-Fi for remote monitoring.
- **Power sources:** Thin-film batteries or energy-harvesting devices for continuous operation.
- **Flexible Substrates and Materials:** Hydrogels, silicon elastomers (PDMS), and polymers provide comfort, skin conformity, and mechanical stability.
- **Adhesives and Protective Layers:** Ensure the device stays securely attached to the skin. Protective coatings prevent moisture ingress, skin irritation, and drug degradation.[9]

Design Aspects of BW-DDS:

- **Biocompatibility:** Materials must be non-toxic, non-irritating, and safe for long-term skin contact.
- **Mechanical flexibility:** Devices should conform to body movements without detachment or damage. [10]
- **Drug Release Control:** Achieved via reservoir design, diffusion membranes, micro-pumps, or stimuli- responsive polymers.
- **Miniaturization:** Electronics and actuators should be compact and lightweight for wearable comfort.
- **Sensor Integration:** Real-time monitoring of physiological signals to adjust drug delivery automatically.
- **Energy Efficiency:** Low-power design ensures long-term operation without frequent recharging.
- **Safety and Redundancy:** Fail-safes to prevent overdose or device malfunction.
- **User Comfort:** Soft, breathable materials, flexible design, and minimal skin irritation.
- **Data Connectivity:** Wireless transmission for remote monitoring, feedback control, and patient adherence tracking.
- **Scalability and Manufacturability:** Design should allow mass production, cost-effectiveness, and reproducibility.
- **Integration with Mobile Apps or Wearables:** Smart Connectivity: BW DDS links with smartphones or wearables via Bluetooth, NFC, or IoT.
- **Mobile Apps:** Show real-time data, control dosing, and send alerts.
- **Wearables:** Sync with sensors (heart rate, glucose, activity) for full patient monitoring.

Real-Time Monitoring and Feedback:

- Continuous Sensing: Biosensors track glucose, pH, temperature, etc.
- **Feedback Control:** Device adjusts drug delivery automatically. Example**:** Smart insulin patches respond to blood glucose changes.
- **AI-Assisted Dosage Adjustment:** AI & Machine Learning: Analyze data to predict and personalize dosing. Benefits**:** Better safety, fewer side effects, and predictive alerts.
- Data Tracking and Patient Compliance
- Data Logging: Records dose, timing, and patient responses:
- Compliance: Reminders and auto-delivery ensure adherence.
- Remote Monitoring**:** Clinicians track patient data in real-time.[11]

Drugs Commonly Delivered via BioWearable Drug Delivery Systems (BW DDS):

Hormones:

- Insulin – diabetes control (pumps, patches)
- Growth Hormone – GH deficiency
- Estrogen, Progesterone, Leuprolide – hormone therapy

Pain Management:

- Fentanyl – chronic pain
- Buprenorphine – opioid therapy
- Lidocaine – local pain relief

Cardiovascular:

- Nitroglycerin – angina
- Clonidine – hypertension

Neurological / Psychiatric:

- Selegiline, Rivastigmine, Donepezil – Parkinson's/Alzheimer's
- Nicotine – smoking cessation
- Scopolamine – motion sickness

Anti-inflammatory / Immunomodulatory:

- Diclofenac, Ketoprofen – arthritis pain
- Methotrexate – autoimmune diseases (experimental)

Vaccines / Biologics:

- COVID-19, Influenza vaccines – microneedle patches
- Monoclonal antibodies – wearable release systems[12]

Others:

- Sumatriptan – migraine
- Local anesthetics – minor procedures
- Anti-cancer drugs – continuous chemo delivery (experimental)

Recent Advances in BW DDS:

1. Dual-Trigger 4D-Printed Smart Polymers
2. Bioelectronics for Localized Delivery
3. Magnetic Electrospun Fibers for Remote-Controlled Release

4. Silk Nanogel Injectors for Targeted Delivery
5. Biohybrid Microrobots for Deep-Tissue Drug Penetration
6. Emerging Research Trend[13]

Integration of AI and Machine Learning:

- Development of Biocompatible Materials
- Advancements in Microfluidics and MEMS
- Remote Monitoring and Control

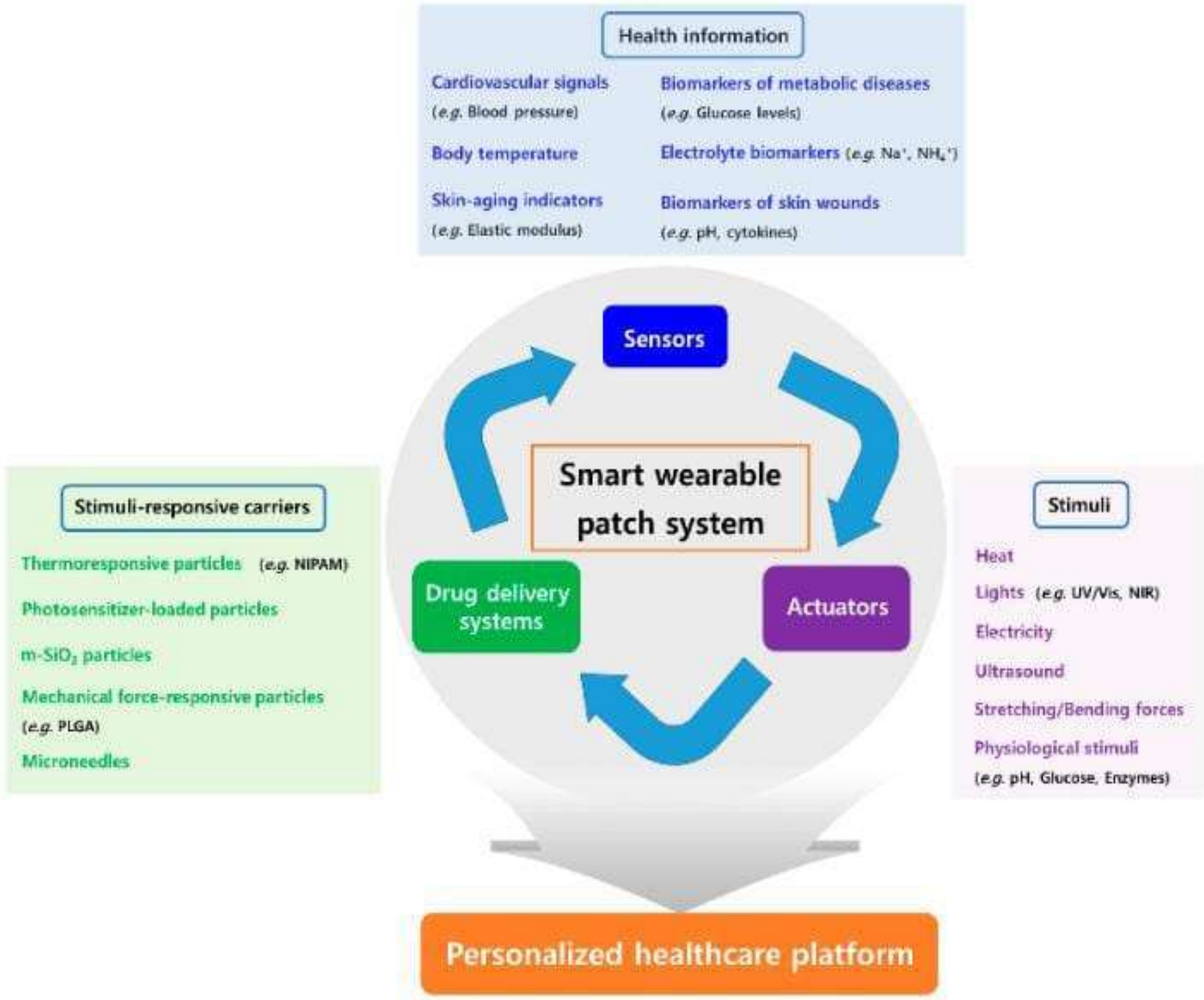

Fig 4: Figure: Schematic Representation of a Smart Wearable Patch System for Personalized Drug Delivery and Health Monitoring

Clinical Studies and Innovations in Drug Delivery Systems:

- **2G Formulations:** Early systems showed limited results; focus has shifted to constant-release, self-regulating, long-term depot, and nano-based systems.
- **Nanomedicines:** Improve targeting, control release, and enhance drug efficacy using nanoparticles.
- **On-Body Injectors:** Offer better patient compliance and comparable or improved outcomes versus IV infusion.[14]

Regulatory and Ethical Considerations in BioWearable Drug Delivery Systems (BW DDS):

Regulatory Considerations:

- **Classification:** BW DDS are combination products (drug + device) requiring dual evaluation by authorities (FDA, EMA, CDSCO).
- **Preclinical Testing:** Check biocompatibility, mechanical safety, and controlled drug release.
- **Clinical Trials:** Must prove safety, efficacy, PK/PD performance, and wear ability.
- **Approval Process:** Requires joint review of drug and device; post-marketing surveillance ensures on-going safety.[16,19]

Ethical Considerations:

- **Patient Safety:** Ensure accurate dosing and minimal side effects.
- **Data Privacy:** Protect sensitive data per HIPAA, GDPR, or local laws.
- **Informed Consent:** Patients must understand risks, data use, and device function.
- **Accessibility:** Promote affordable access and equity in all regions.
- **Device Reliability:** Devices should be safe, user-friendly, and error-proof to protect patients.

Emerging Technologies in BioWearable Drug Delivery Systems (BW DDS):

- **4D-Printed Smart Polymers:** Developed at IIT Bhili, these materials change shape with temperature or ph. Used in minimally invasive surgeries, bio-robots, and adaptive drug delivery.
- **On-Body Injectors (OBIs):** Deliver large or viscous drugs subcutaneously.
- **Example:** Phillips-Midsize OBI delivers up to 5 mL of 20 cP liquid in under a minute. Supports modular and faster drug delivery.
- **Wearable Biosensors and Smart Patches:** Monitor glucose, blood pressure, and sweat biomarkers. Combine sensing, feedback, and controlled drug release for personalized therapy. [17,18]

Future Outlook:

The future of BioWearable Drug Delivery Systems (BW DDS) lies in combining advanced materials, miniaturized electronics, and personalized medicine.

Next-generation systems will provide greater precision, adaptability, and comfort, making treatments more effective and accessible.

Fig 5: On-Body Injector (OBI) Device Used in BioWearable Drug Delivery Systems (BW DDS)

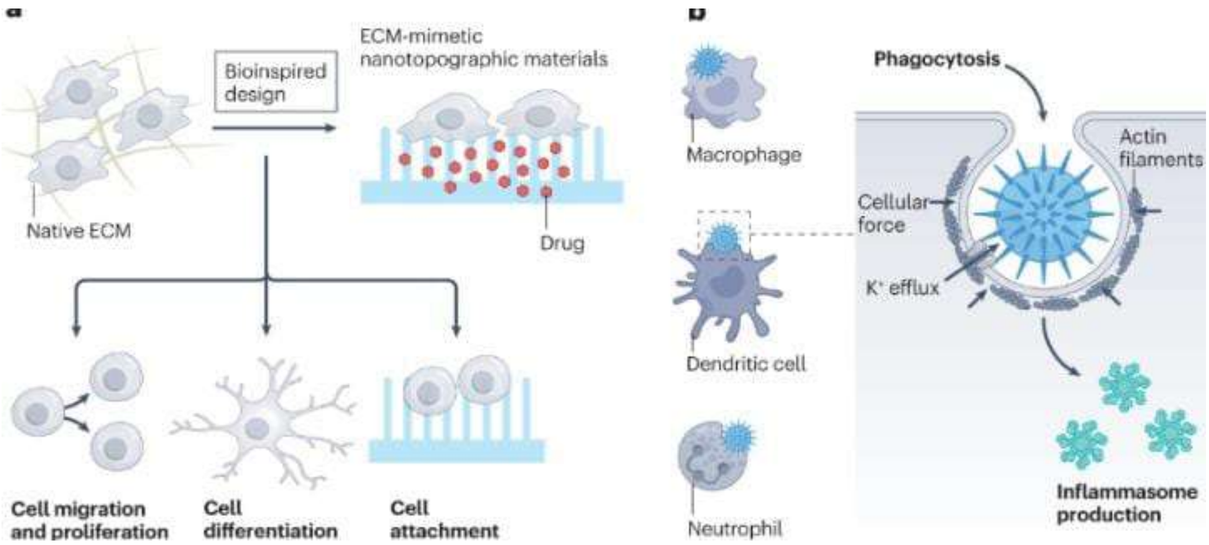

Fig 6: Figure: Bio inspired Nano topographic Materials for Drug Delivery and Immune Cell Interaction

Conclusion:

BioWearable drug delivery systems offer precise, controlled, and continuous drug administration, improving therapeutic outcomes and patient compliance. Integration of sensors, electronics, and AI enables real-time monitoring and personalized therapy. Although challenges like biocompatibility, durability, and regulatory hurdles remain, advances in materials and wearable design are addressing these issues. BW DDS have significant potential in chronic disease management, personalized medicine, and next-generation healthcare.

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