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TO APPROACH TO PERSONALISED MEDICINE

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ABSTRACT

Conventional drug delivery systems often lack the ability to adapt to the individual needs of patients. Feedback-regulated systems, an emerging field, aim to address this by incorporating responsive mechanisms that adjust drug release based on real-time physiological or disease- specific feedback signals, thereby addressing this issue. These systems hold immense potential for personalized and precise therapy, offering several advantages: Enhanced therapeutic efficacy: By adjusting drug release based on individual needs, feedback-regulated systems can potentially achieve optimal therapeutic levels while minimizing side effects. Reduced dosing frequency Continuous monitoring and adaptation can allow for less frequent dosing, improving patient adherence and reducing the risk of missed doses, thereby improving treatment compliance. Improved safety:

The ability to respond to changes in a patient's condition can help prevent overdosing or underdosing, leading to safer treatment regimens and better patient outcomes.

Despite the promise, challenges remain in developing robust and reliable feedback mechanisms, ensuring biocompatibility and safety, and navigating regulatory hurdles, which must be addressed to fully realize the potential of feedback-regulated drug delivery systems. Nevertheless, ongoing research suggests that feedback-regulated drug delivery systems have the potential to revolutionize personalized medicine, offering tailored and effective treatments for a wide range of diseases. This could significantly improve patient outcomes.

Keyword: Feedback-Regulated Drug Delivery Systems , polymers, stimulus.

1. INTRODUCTION

Feedback-Regulated Drug Delivery Systems: A New Era of Personalized Therapy Traditional drug delivery systems, while effective in many cases, often have limitations.These limitations include: Inability to adapt: Current systems often deliver a fixed dose regardless of individual needs, potentially leading to underdosing or overdosing. Limited efficacy: A constant dose may not maintain optimal therapeutic levels throughout treatment, hindering efficacy.Side effects: Maintaining therapeutic levels may lead to unwanted side effects for some patients due to individual variations in drug metabolism and response.To address these challenges, a new frontier in drug delivery is emerging: feedback-regulated drug delivery systems.

These novel systems incorporate intelligent mechanisms that can respond to real-time information about the patient's condition. Imagine a system that continuously monitors a patient's biomarkers, such as blood sugar levels or tumor size, and adjusts the drug release rate accordingly. This allows for personalized therapy, tailoring the treatment to the unique needs of each individual.

The potential benefits of feedback-regulated systems are numerous. Improved therapeutic efficacy: By adjusting the dose based on individual needs, these systems can potentially achieve optimal therapeutic levels while minimizing side effects. Enhanced patient compliance: Less frequent dosing, due to continuous monitoring and adaptation, can improve patient adherence to treatment protocols. Increased safety:

The ability to respond to changes in a patient's condition can help prevent overdosing or underdosing, leading to safer treatment regimens.

While still under development, this innovative technology holds immense promise for revolutionizing personalized medicine. Research efforts are underway to overcome challenges such as developing robust feedback mechanisms, ensuring biocompatibility and safety, and navigating regulatory pathways. The future of drug delivery may be heading towards a more precise and patient-centric approach, all thanks to the potential of feedback-regulated systems.

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2. MECHANISM OF FRDDS

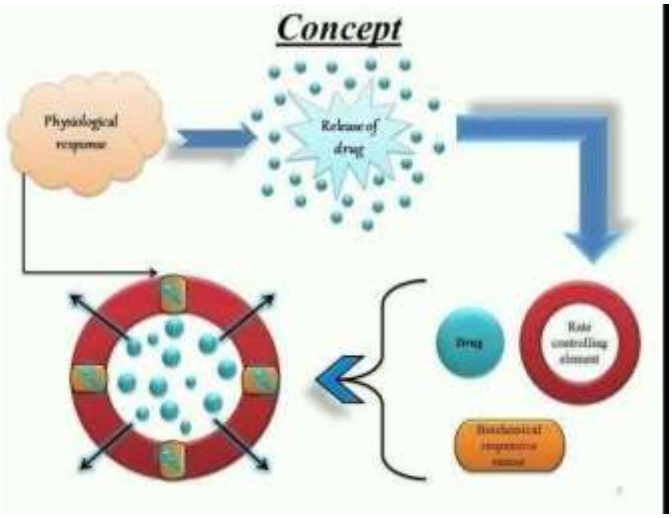

Fig.1: Mechanism of feedback-regulated drug delivery systems.

Feedback-regulated drug delivery systems are still in the early stages of development, but researchers are exploring various mechanisms to achieve real-time adjustments in drug release. Here are some potential mechanisms:

A. Bioresponsive Materials: These materials can change their properties based on biological stimuli, such as:

- **pH**: Certain polymers can swell or degrade at specific pH levels, releasing the drug in response to changes in the surrounding environment (e.g., tumor acidity).
- **Enzymes**: Drug-polymer conjugates can be designed where enzymes present in specific tissues cleave the bond, releasing the drug in the target location.
- **Temperature**: Temperature-sensitive polymers can release their payload upon reaching a specific temperature (e.g., hyperthermia therapy).
- **Glucose**: Systems sensitive to glucose levels can be used for targeted insulin delivery in diabetes management.

B. External stimuli: These systems utilize external controls to adjust drug release:

- **Magnetic nanoparticles:** By applying an external magnetic field, the nanoparticles can be manipulated to release the drug in a controlled manner. Light-activated systems: Light-sensitive polymers can be triggered to release the drug upon exposure to specific wavelengths of light. ii. **Ultrasound:** Ultrasound waves can be used to trigger the release of drugs from a carrier system.

C. Biosensors and feedback loops: These systems employ integrated sensors and control mechanisms.

- **Microfluidic chips:** These microfluidic devices can house miniaturized sensors that detect the target biomarker and adjust drug release through microvalves or other mechanisms.
- **Nanoporous materials:** These materials can encapsulate drugs and integrate sensors that respond to specific biological signals, triggering the release mechanism.
- **Closed-loop systems:** These technologically advanced systems utilize continuous monitoring of physiological parameters and integrate them withcontrol algorithms to adjust drug release in realtime.

Polymers for Feedback-Regulated Drug Delivery Systems with General Discrimination:

polycarbonate. A basic medication is included in the formulation, along with a binder, a pH- dependent polymer that is a water-soluble salt of alginic acid (such as sodium or potassium alginate), a pH-independent hydrocolloid, and a gelling agent (such as HPMC, methyl cellulose, or HPC).In order to create hollow microspheres that can float on stomach fluid and deliver their pharmacological payload for a prolonged period of time, polymers like these are utilized.

Table 1: Polymers name with their stimuli and examples.

Sr.No.	Polymer Name	scriminatig Stimulus	Example
1	(Nisopropylacrylamid e) (PNIPAAm)	Temperature	Releases drug above a specific temperature (e.g.,hyperthermia therapy)
2	Poly(methacrylic	PH	Releases drug in acidic environments (e.g., tumor targeting)

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3	Chitosan	PH and enzymes	Degrades in acidic environments and can be cleaved by specific enzymes in targeted tissues
4.	Dextran	PH and enzymes	Similar to chitosan, can be designed to respond to pH and enzymatic cues
5	Poly(γ-glutamic acid) (γ-PGA)	PH and enzymes	Biodegradable polymers are responsive to changes in pH and,can be enzymatically degraded.

Classification of Feedback-Regulated Drug Delivery Systems:

A. Bioerosion-Regulated Dreg Delivery System

B. Bioresponsive Drug Delivery Systems

C. Self-Regulating Drug Delivery Systems

A) Bioerosion-Regulated Dreg Delivery System:

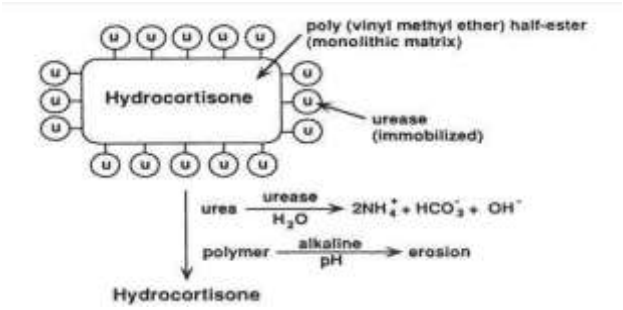

Fig.2:Cross-sectional view of a bioerosion-regulated drug delivery system, a feedback- regulated drug delivery system, showing the drugdispersed monolithic bioerodible polymer matrix with surfaceimmobilized ureases.

Heller and Trescony explored the concept of feedback-regulated drug delivery by developing a system that utilizes bioerosion as the control mechanism. This system comprises a drug- dispersed matrix fabricated from polyvinyl methyl ether half-ester and coated with a layer of immobilized urease. In a near-neutral pH environment, the polymer exhibits minimal erosion. However, in the presence of urea, the immobilized urease catalyzes its conversion to ammonia, leading to a localized increase in pH. This pH shift triggers rapid degradation of the polymer matrix, facilitating the release of encapsulated drug molecules.

B) Bioresponsive Drug Delivery Systems

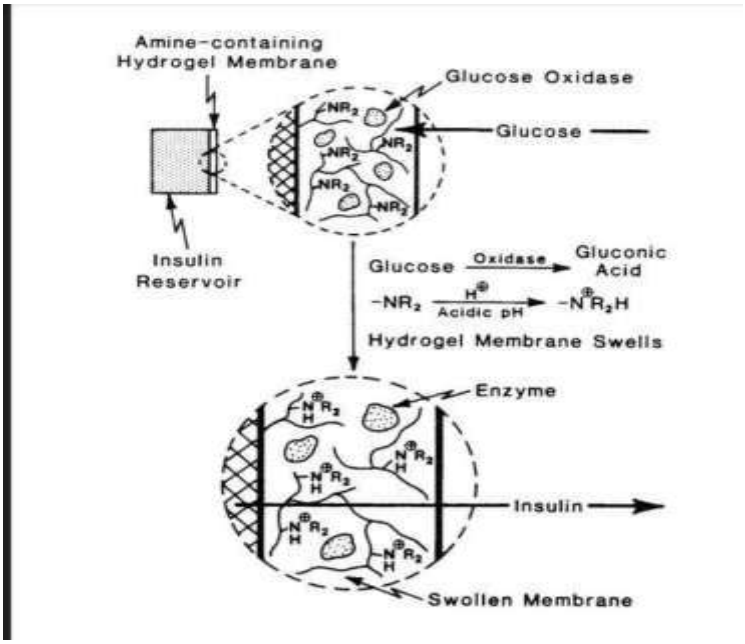

Fig. 3: Cross-sectional view of a bioresponsive insulin delivery system, a feedback- regulated drug delivery system, showing the glucose oxidaseentrapped hydrogel membrane constructed from an amine- containing hydrophilic polymer. The mechanism of insulin release in response to the influx of glucose is also illustrated

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Researchers have developed a bioresponsive drug delivery system based on feedback-regulated release. This system utilizes a drug reservoir encased within a special membrane. The key feature of this membrane is its responsiveness to changes in the surrounding environment, specifically the concentration of a particular biomolecule. An example of this system is a glucose-triggered insulin delivery device. In this case, the insulin reservoir is encapsulated in a hydrogel membrane containing specific chemical groups. These groups act as a "gatekeeper," controlling the release of insulin. When the target biomolecule, in this case, glucose, enters the surrounding tissue, it interacts with the membrane.** This interaction triggers a specific chemical reaction, leading to a change in the properties of the membrane. As a result, the previously closed membrane becomes "unlocked," allowing insulin to pass through. Therefore, the amount of insulin released is directly linked to the concentration of glucose present, showcasing the bioresponsive nature of the system. This approach offers a more precise and targeted drug delivery method compared to traditional methods.

C) Self-Regulating Drug Delivery Systems:

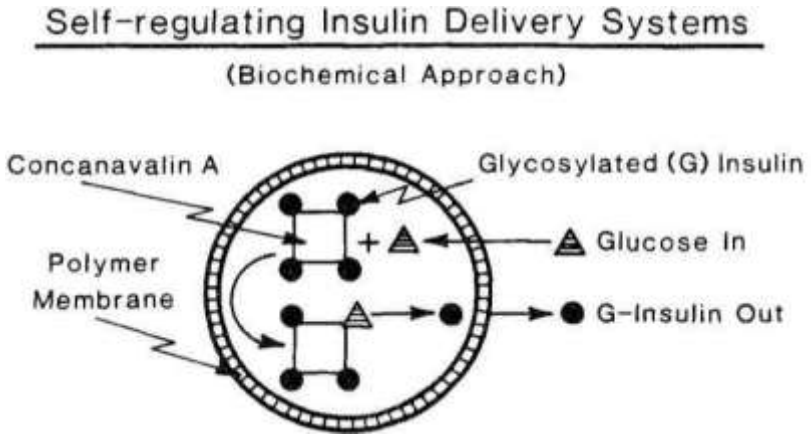

Fig. 4: Various components of a self-regulating insulin delivery system, a feedback- regulated drug delivery system, and its control of blood glucose levels in pancreatectomized dogs.

This type of drug delivery system relies on a "lock and key" mechanism: drugs are trapped within a membrane, and a specific molecule acts as a key to unlock the release. This key molecule, often found in the surrounding tissue, competes with the drug for binding sites on the "lock" structure. The first example involved insulin linked to sugar molecules, which bind to lectin molecules in the system. When blood sugar enters, it competes with the attached sugar, releasing insulin. While effective, the release was not perfectly proportional to sugar levels. A later iteration used a complex of insulin and another molecule, concanavalin A, encapsulated within a membrane. When glucose enters, it competes with this complex, causing controlled release of insulin. This system offers more precise control based on the surrounding glucose concentration.

Factors Affecting Feedback-Regulated Drug Delivery Systems: Several factors can influence the efficacy and performance of feedbackregulated drug delivery system

1. **Design and Development:** Polymer properties, feedback mechanism design, release mechanism efficiency, drug loading and stability, biocompatibility of all components, system stability, and degradation.2. Biological Considerations: Target specificity, biological barriers, immune response.
2. **Manufacturing and Regulatory Challenges:** Scalability and cost, regulatory hurdles.
3. **Ethical Considerations:** Patient safety, data privacy.
4. Patient compliance
5. Cost-effectiveness

Evaluation Parameters for feedback-regulated drug delivery systems:

A. In Vitro Evaluation Parameters :

- System Stability
- Chemical stability of the drug Stability of the feedback mechanism Physical stability of the system components.
- Responsiveness Sensitivity of the sensor Accuracy of the sensor Speed of drug release adjustment.
- Biocompatibility
- Cytotoxicity
- Hemocompatibility

B. In Vivo Evaluation Parameters

- Pharmacokinetics
- Drug release rate
- Drug absorption
- Drug distribution
- Drug metabolism
- Concentration-effect relationship
- Therapeutic efficacyafety
- Local tissue reactions
- Systemic toxicity
- Immunogenicity

C. Clinical Evaluation Parameters

- Efficacy
- Disease-specific outcome measures

Table 2: Advantages and Disadvantages of FRDDS

Advantages	Disadvantages
Enhanced Therapeutic Efficacy	Increased Complexity
Increased Patient Complianc	Regulatory hurdles
Potential for Cost-Effectiveness:	Cost and accessibility
Navigating complex regulatory pathways for novel technologies	Potential Risks and Uncertainties

Application:

1. **Cancer therapy:** Targeted drug delivery systems can be designed to release drugs specifically within tumors based on the unique tumor microenvironment (e.g., pH, presence of specific enzymes). This can improve therapeutic efficacy while minimizing side effects on healthy tissues. Controlled dosing based on tumor progression: Real-time

   monitoring of tumor size or specific biomarkers can allow for adjustments in drug release, optimizing treatment based on individual response.

2. **Chronic disease management:** Diabetes management: Glucose- responsive systems can deliver insulin in response to fluctuating blood sugar levels, providing a more personalized and effective approach to managing diabetes. Cardiovascular disease: Systems can monitor and respond to changes in blood pressure, heart rate, or specific markers like cholesterol, adjusting medication delivery to maintain optimal cardiovascular health.

   Chronic pain management: Systems can deliver pain medication based on real-time pain intensity signals, providing targeted relief and potentially reducing overall medication use.

3. **Neurodegenerative diseases:** Targeted delivery to the brain systems can be designed to overcome the blood-brain barrier and deliver drugs directly to specific brain regions affected by neurodegenerative diseases like Alzheimer's or Parkinson's, potentially improving treatment efficacy.

4. **Infectious diseases:** Antimicrobial delivery with feedback: Systems can be designed to respond to changes in bacterial or viral load, adjusting the release of antibiotics or antiviral medications to combat infections more effectively and potentially reduce the emergence of drug resistance.

   Personalized treatment based on pathogen identification: Feedback mechanisms may be able to identify specific pathogens and adjust the drug release accordingly, leading to more targeted and effective treatment of various infectious diseases.

3. CONCLUSION

Feedback-regulated drug delivery systems, though still under development, offer a glimpse into the future of personalized and adaptive medicine. These systems hold the potential to revolutionize treatment by optimizing drug levels. By continuously monitoring and adjusting drug release based on real-time feedback, these systems can potentially maintain therapeutic drug levels within the body, minimizing both underdosing and over-dosing, ultimately leading to improved treatment outcomes.

Minimizing side effects: By ensuring precise drug delivery, these systems can potentially reduce the risk of adverse reactions often associated with traditional drug delivery methods, thereby improving patient safety and comfort.

Personalizing treatment: By tailoring drug release to the specific needs and biological responses of each patient, these systems have the potential to revolutionize the way chronic diseases are managed, offering a more individualized and effective approach to treatment.Overall, the future of FRDDS is bright, with the potential to revolutionize personalized medicine by offering targeted, adaptable, and efficient drug delivery, ultimately lead to improved patient outcomes and a paradigm shift in disease management.Overall, the future of FRDDS is bright, with the potential to revolutionize personalized medicine by offering targeted, adaptable, and efficient drug delivery, ultimately leading to improved patient outcomes and a paradigm shift in disease management.

4. FUTURE DIRECTIONS

The future of feedback-regulated drug delivery systems (FRDDS) is brimming with exciting possibilities:

- **Enhanced Biomaterials and Fabrication:** Development of advanced biomaterials with improved biocompatibility, responsiveness, and controlled release mechanisms is crucial. This includes exploring nanocarriers and stimuli- responsive polymers that can adapt to specific biological cues.
- **Integration of Biosensors and Advanced Diagnostics:** Seamless integration of biosensors and advanced diagnostic tools within FRDDS is essential. These sensors will allow real-time monitoring of various physiological parameters (e.g., blood sugar, inflammatory markers) and provide crucial feedback for regulating drug release.
- **Artificial Intelligence and Machine Learning:** Leveraging artificial intelligence (AI) and machine learning (ML) algorithms can significantly enhance FRDDS functionality. These algorithms can analyze complex biological data from sensors and patient history to predict individual needs and personalize drug release patterns in real-time.
- **Closed-Loop Systems and Patient Integration:** The future envisions closedloop FRDDS, where the system continuously collects feedback, analyzes data, and adjusts drug release automatically, minimizing human intervention.

  Additionally, integration with wearable devices and smartphone apps can empower patients to actively monitor their treatment progress and potentially participate in decision-making.
- **Addressing Challenges:** Addressing current challenges remains critical. Technical development: Designing reliable and biocompatible mechanisms for real-time feedback and controlled drug release remains an active area of research. Extensive testing and evaluation are crucial to ensure the safety and efficacy of these complex systems before widespread adoption.

5. REFERENCES

[1] Bhat M, Shenoy DS, Udupa N, Srinivas CR. Optimization of delivery of betamethasone- dipropionate from skin preparation. Indian Drugs. 1995;32:211–4. [Google Scholar]

[2] Misra A, Pal R, Majumdar SS, Talwar GP, Singh O. Biphasic testosterone delivery profile observed with two different transdermal formulations, Pharm Res. 1997;14:1264–08 PubMed] [Google Scholar]

[3] Thacharodi D, Rao KP. Rate-controlling biopolymer membranes as transdermal delivery systems for nifedipine: Development and in vitro evaluations. Biomaterials. 1996;17:1307–11. [PubMed] [Google Scholar]

[4] Nanda A, Khar RK. Permeability characteristics of free films studied using drugs such as diltiazem hydrochloride and indomethacin. Drug Dev Indian Pharm. 1994;20:3033–44. [Google Scholar]

[5] Mukhopadhyay A, Mukhopadhyay B, Basu K. Circumvention of multidrug resistance in neoplastic cells through scavenger receptor-mediated drug delivery. FEBS Lett. 1995;276:95–8. [PubMed] [Google Scholar]

[6] Nanda A, Khar RK. Pulsed mode constant current iontophoretic transdermal delivery of propranolol hydrochloride in acute hypertensive and normotensive rats. Indian Drugs. 1998;35:274–80. [Google Scholar]

[7] Murthy SN, Shobha Rani HS. Comparative pharmacokinetic and pharmacodynamic evaluation of oral vs transdermal delivery of terbutaline sulphate. Indian Drugs. 1998;35:34–6. [Google Scholar]

[8] Rao MY, Vani G, Chary BR. Design and evaluation of mucoadhesive drug delivery systems. Indian Drugs. 1998;35:558–65. [Google Scholar]

[9] Murthy NS, Satheesh M. Enhancer synergism of propylene glycol and PEG -400 in terbutaline sulphate transdermal drug delivery systems. Indian Drugs. 1997;34:224– [Google Scholar]

[10] Tatapudy H, Madan PL. Benzoyl peroxide microcapsules I. Preparation of core material. Indian Drugs. 1995;32:239–48. [Google Scholar]

[11] Kshirsagar NA, Gokhale PC, Pandya SK. Liposomes as a drug delivery system in leishmaniasis. J Assoc Physicians India. 1995;43:46–8. [PubMed] [Google Scholar]

[12] Recent advances in self-regulated drug delivery devices.

[13] J Control Release 2015Wicki A, Witzigmann D, Balasubramanian V, Huwyler J. nanomedicine in cancer therapy: challenges, opportunities, and clinical applications. J Control Release 2015;200:138–57

[14] Novel drug delivery systems. Second Edition, mused aid Expanded Y i e W . Controlled Drug-Delivery Research Center College of Pharmacy Rutgers University Piscataway, New Jersey