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NEW INNOVATIVE TECHNIQUE CELLULOSE PAPER-BASED SMART FILMS: A REVIEW

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Abstract
This document explores the evolution of medicine from ancient practices to modern pharmaceuticals and focuses on the development and application of cellulose paper-based smart Films for API delivery in disease management. It begins with a historical overview of medical practices and the significance of oral drug administration. The core of this document introduces "Smart Films" technology, a groundbreaking method to improve the solubility and dissolution rate of weakly water-soluble pharmaceutical drugs, with a focus on API-loaded smart films. The preparation process, sterilization of paper and production of API-loaded smart films and tablets are described in detail. The application of these cellulose paper-based smart films in diabetes management is emphasized, highlighting their enhancement in drug release capabilities and patient-centric advantages. Furthermore, the document envisions future directions in smart film technology, including personalization based on physiological responses and genetic makeup, nanotechnology integration, sustainable materials, and interdisciplinary collaboration. The role of these innovations in advancing the field of drug delivery and their potential to improve patient outcomes is discussed. This comprehensive exploration of cellulose paper-based smart films for API delivery offers valuable insights into the future for the management of diabetes and pharmaceutical advancements.

INTRODUCTION

Since ancient times, humans have practiced medicine through various methods, including bone remains, drawings, paintings, and surgical instruments. Early medicine was based on religion, magic, and rituals, with witches and alchemists using herbs, vegetables, and cure mixtures. In ancient Egypt, preserved mummies revealed diseases in the population, such as parasitic infections, arthritic conditions, bladder stones, and tuberculosis. Greek medicine had a significant impact, using reasoning and observations to understand health and disease. Hippocrates of Kos, the founder of Western medicine, introduced prognosis, ethics, and diagnosis. Over time, ideas about health, illness, and death have evolved across diverse cultures, and the professional medicine now practiced has altered how diseases are approached and treated [1-6].

Oral drug administration is the preferred method for treating gastrointestinal tract (GIT) problems and distributing drugs systemically. It offers low infection risk, low sterility requirements, and cost savings. Oral delivery systems are simple, non-invasive, and practical for self-administration, leading to excellent patient compliance. They can be made in solid dosage forms like tablets, capsules, or granular or liquid forms like suspensions, emulsions. Aqueous solubility, stability, dissolution rate, permeability, first-pass metabolism, pre-systemic metabolism, and drug molecules susceptibility to efflux mechanisms all impact the effectiveness of oral drug delivery, resulting in high oral bioavailability [7-11].

By integrating poorly soluble drugs in an amorphous form into the cellulose matrix, cellulose paper-based smart membranes can increase the solubility, permeability, and bioavailability of certain drugs. They can also be used in many applications, including smart devices, actuators and sensors.

Tablets are solid dosage forms which could be flat or biconvex and are prepared by compressing drug and other ingredients, with or without diluent. They vary in bulk and quantity depending on the medicine substance and intended mode of use for the management of disease. Pharmaceutical excipients are substances beside the active pharmaceutical ingredient (API) that have been

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properly assessed for safety and are purposefully included in drug delivery systems. Tablets are prepared using three methods: wet granulation, dry granulation, and direct compaction. Wet granulation involves weighing, mixing, granulating, filtering, drying, lubricating, and compacting tablets. Dry granulation or double compaction eliminates the steps involved in powder mass formation, and direct compaction involves direct compression of the powder material into pellets. Tablets containing 25% or less of the drug may be formulated with an appropriate diluent as a carrier or drug carrier [12-16].

SMART FILM TECHNOLOGY

Lemke and his colleagues first unveiled the SmartFilms technology in 2016 as a ground-breaking method for improving the solubility and dissolution rate of the weakly water-soluble pharmaceutical drugs [17]. The term "SmartFilms" refers to sheets of paper made from cellulose in which the API has been loaded in an amorphous state inside the pores of the cellulose matrices. A weakly water-soluble drug is dissolved in the proper solvent to create smartFilms, which are then dried after the drug-filled solution has been added to cellulose-based paper [17, 18]. As a potential method for improving the solubility of pharmaceuticals that are not very water-soluble, SmartFilms technology provides a number of benefits. Amorphous states of several pharmaceutical drugs could be attained by smartFilms lasting at least 18 months, demonstrating their long-term stability [17, 18].

Administration of paper (i.e., smartFilms) is not patient-friendly, while being a promising oral medication delivery technology. Incorporating smartFilms into the proper oral dosage forms can thereby increase patient adherence to the cutting-edge technology. According to preliminary findings, smartFilms can be compacted into tablets without the use of any additional excipients [17, 18]. The idea of compressing several types of unloading paper (such as disposable handkerchiefs, kitchen rolls, cleaning cloths, cosmetic facial tissues, and coffee filters) into tablets was examined in the first comprehensive investigation by Stumpf and Keck [19].

The creation of various drug-loaded smartFilm tablets was then reported in a number of studies, and the characteristics of the tablets that were created were also investigated [19-22].

Further the study of BCS class II (i.e., low solubility and high permeability) efavirenz, an anti-HIV drug has been done using the co-solvency technique to prepare smartFilm tablets. According to the study's findings, efavirenz-loaded smartFilm tablets made from toilet paper complied with European Pharmacopoeia standards and displayed a better efavirenz release profile over 180 minutes than alternative formulations. Additionally, according to the stability experiments, the efavirenz-loaded smartFilm tablets were stable over a two-month period [23].

CO-SOLVENCY

Co-solvency is a method that combines a non-polar solvent with a water-miscible or partially miscible solvent to improve solubility. Commonly used in procedures like precipitation, pH correction, and solid dispersions, it is used in parenteral fluids. SmartFilm tablets' bioactivity and dissolution rate can be studied for poorly water-soluble medications using co-solvency techniques [23, 24-26].

METHOD OF PREPERATION

Sterilization of paper

It is very much possible to use and sterilize various grades of papers like (kitchen roll, paper, facial tissue paper, and handkerchief paper) and is done in a hot air oven at temperatures of about 150 and 200 ° C for 10 minutes before the next steps are carried out. The sterilized papers were then used for the next steps [23].

Production of API loaded smart film

The first step is to produce the solution of API using proper co-solvent. The obtained API solution is loaded onto precut paper sheets of 6.5×6.5 cm^2 with independent mass of roughly about 150-200mg by using micropipette. These sheets of paper are then left outside for the purpose of drying, and then the process was repeated a number of times until required quantity of the API-loaded smartFilms are produced [19].

Production of API loaded smartFilm tablet

The dried smartFilms are then cut into smaller pieces of 1×1cm^2. The smartFilms are manually feed into the tablet press cavity. And then compacted with a compression force of 30kN with an 8 mm flat-faced punch to form flat faced smartFilm tablets. By incorporating the tablet test parameters from the Indian Pharmacopeia 8.0, the qualities of the tablets produced were assessed appropriately [19].

APPLICATION

One promising avenue lies in the development and application of cellulose paper-based API smart films, which combine the advantages of cellulose as a biocompatible material with the drug delivery capabilities of smart films.
Cellulose, derived from renewable sources like wood pulp and cotton, has gained significant awareness in drug

delivery systems due to its biocompatibility, decomposable nature, and less toxicity level. Cellulose-based materials offer a suitable matrix for drug delivery, ensuring patient safety and environmental sustainability. Cellulose paper-based API smart films are designed to release the drug in an efficient manner as compared to conventional drug formulation, responding to specific stimuli. These stimuli can include changes in pH, temperature, or hormonal levels. The precision of drug release enhances therapeutic efficacy while minimizing the risk of medications.

The application of cellulose-based smart films aligns with the shift towards patient-centric care in disease management. Patients can self-administer API via these films, offering convenience and reducing the need for frequent injections or oral medication. Additionally, the flexibility of cellulose paper allows for easy customization of film size and shape to accommodate individual patient preferences.

One of the advantages of API-based smart films is the potential to reduce side effects associated with the medication. The release mechanism mitigates the risk of overdose and gastrointestinal disturbances commonly observed with conventional oral tablets.

POPULARITY OF CELLULOSE IN SMARTFILMS

Cellulose-based films have gained prominence in oral drug delivery due to their unique properties. Here are various technologies and applications of cellulose-based films in this specific area:

- Oral Drug Delivery: Cellulose-based OTFs may be the most notable oral medication delivery method. These thin, flexible films dissolve quickly in the tongue and administer medications in an easy-for-patients way. For those who have trouble swallowing medicines, they are extremely helpful.
- Mucoadhesive Films: Mucoadhesive characteristics can be added to cellulose-based films. They stick to the oral cavity mucous membranes, delaying medication release and increasing bioavailability.
- Buccal Drug Delivery: Drugs can be absorbed through the buccal mucosa (inside cheek) when delivered through buccal using films. This method results in quick drug absorption because it skips the digestive system and liver.
- Sublingual Films: Sublingual films are used under the tongue for rapid drug absorption, much like buccal films are. Films made of cellulose work well for this.
- Transmucosal Drug Delivery: Drugs can be delivered transmucosally via films, which allows for a quicker beginning of action than with conventional oral formulations.
- Hydrophilic Matrices: In order to regulate the rate of drug release and improve dissolve qualities, hydrophilic matrices can be made using modified cellulose derivatives in tablet formulations.
- Biodegradable Films: Films made of cellulose are environmentally beneficial medication delivery devices since they are biodegradable and produce less plastic waste.

FUTURE DIRECTIONS

Future direction of the project holds immense promise, driven by the convergence of advanced technologies and a growing need for more efficient and patient-centric treatments. Future smartFilms will likely move towards greater personalization. Tailoring drug release rates and dosages based on an individual's unique physiological responses and lifestyle factors could optimize treatment outcomes. Advancements in pharmacogenomics may enable the development of API smart films that are finely tuned to a patient's genetic makeup, ensuring not only efficacy but also minimizing side effects.

The use of nanotechnology in smart film formulations may become more prevalent, offering improved drug delivery precision, stability, and bioavailability. Sustainable and biodegradable materials for smart films could reduce environmental impact and improve patient compliance. Future research will need to address evolving regulatory requirements to ensure the safety and effectiveness of these innovative drug delivery systems. Interdisciplinary collaboration between pharmaceutical scientists, material engineers, data analysts, and healthcare providers will be crucial to advancing the field.

CONCLUSION

In conclusion, the evolution of medicine, from traditional methods to contemporary medications, has paved the way for innovative developments in drug distribution. Among these advancements, cellulose paper-based smart film tablet stand out as a promising solution for efficient and patient-centric drug delivery.

Improved Drug Release Capabilities: Cellulose paper-based smart film tablet enhance drug release efficiency, ensuring timely and controlled delivery of active pharmaceutical ingredients (APIs). These smart film tablet can be customized to release medications at specific rates, optimizing therapeutic outcomes.

Patient-Centric Benefits: Patients benefit from the convenience and ease of using smart film tablet. Unlike conventional pills, smart film tablet are practical and user-

friendly. Accurate dosages are guaranteed, promoting adherence to treatment plans and improving patient outcomes.

Personalized Therapy: Smart film tablet allow tailoring of dosages to individual patient needs. This personalized approach enhances treatment effectiveness. By providing accurate and customized drug delivery, smart film tablet contribute to better disease management.

Environmental Sustainability: Cellulose paper, the primary material for smart film tablet, is eco-friendly and sustainable. Choosing smart film tablet over traditional pills reduces plastic waste and supports environmental conservation.

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CONSENT FOR PUBLICATION

The authors declare no conflict of interest.

COMPETING INTERESTS

The authors declare that they have no competing interests.

REFERENCES

[1] Selin H, Shapiro H, editors. Medicine across cultures: history and practice of medicine in non-western cultures. Berlin Heidelberg New York: Springer; 2003. pp. 27–47.

[2] Nunn JF. Ancient Egyptian medicine. Norman OK: University of Oklahoma Press; 2002.

[3] Grammaticos PC, Diamantis A. Useful known and unknown views of the father of modern medicine, Hippocrates and his teacher Democritus. Hell J Nucl Med. 2008;11(1):2–4.

[4] Yapijakis C. Hippocrates of Kos, the father of clinical medicine, and Asclepiades of Bithynia, the father of molecular medicine. Review. In Vivo (Brooklyn). 2009;23(4):507–14.

[5] França K, Chacon A, Ledon J, Savas J, Nouri K. Pyschodermatology: a trip through history. An Bras Dermatol. 2013;88(5):842–3. https://doi.org/10.1590/abd1806-4841. 20132059.

[6] Lotti TM. The renaissance of dermatology: selected concepts beyond the skin. Arch Dermatol. 2000;136(1):69–70.

[7] Arshad, M.S.; Zafar, S.; Yousef, B.; Alyassin, Y.; Ali, R.; AlAsiri, A.; Chang, M.-W.; Ahmad, Z.; Elkordy, A.A.; Faheem, A. A review of emerging technologies enabling improved solid oral dosage form manufacturing and processing. Adv. Drug Deliv. Rev. 2021, 178, 113840, doi:10.1016/j.addr.2021.113840.

[8] Alqahtani, M.S.; Kazi, M.; Alsenaidy, M.A.; Ahmad, M.Z. Advances in oral drug delivery. Front. Pharmacol. 2021, 12, 618411, doi:10.3389/fphar.2021.618411.

[9] Homayun, B.; Lin, X.; Choi, H.-J. Challenges and Recent Progress in Oral Drug Delivery Systems for Biopharmaceuticals. Pharmaceutics 2019, 11, 129, doi:10.3390/pharmaceutics11030129.

[10] Hua, S. Advances in Oral Drug Delivery for Regional Targeting in the Gastrointestinal Tract - Influence of Physiological, Pathophysiological and Pharmaceutical Factors. Front. Pharmacol. 2020, 11, 524, doi:10.3389/fphar.2020.00524.

[11] Savjani, K.T.; Gajjar, A.K.; Savjani, J.K. Drug solubility: importance and enhancement techniques. Int. Sch. Res. Notices 2012, 2012, 1–10, doi:10.5402/2012/195727.

[12] Leon Lachman, Herbert A. Lieberman, Joseph L. Kanig: The theory and Practice of Industrial Pharmacy, Varghese publication house, 3rd edition, 1990, 293-373.

[13] Herbert A. Liberman, Martin M. Rieger and Gilbert S. Banker, pharmaceutical dosage forms: Tablets; volume-I.

[14] Al-Achi A (2019) Tablets: A Brief Overview. Journal of Pharm Practice and Pharmaceutical Science. 2019(1): 49-52.

[15] Nagashree K. Solid dosage forms: Tablets. Research and Reviews: Journal of Pharmaceutical Analysis. 2015.

[16] Ubhe, Tejaswi Santosh, and Preeti Gedam. "A Brief Overview on Tablet and It's Types." Journal of Advancement in Pharmacology 1.1.

[17] Lemke, S.; Strätling, E.J. SmartFilms-oral and peroral films for optimized delivery of nanoparticulate or amorphous drugs. Controlled Release Society Local Chapter, Saarbrücken/Germany 2016, 7

[18] Lemke S, Strätling EJ, Welzel, HP. Cellulose faser basierte Trägermatrices (smartFilms) zur Applikation von Inhaltsstoffen sowie deren Herstellung. German Patent Application DE102016000541A1 2017.

[19] 19. Stumpf, F.; Keck, C.M. Tablets made from paper. Int. J. Pharm. 2018, 548, 812–819, doi:10.1016/j.ijpharm.2018.05.071.

[20] Stumpf F. Tabletten aus Papier – tablets made from paper – zur oralen Applikation schwerlöslicher Wirkstoffe. PhD-thesis; Philipps-Universität Marburg, Marburg, 2019.

[21] Ornik J, Knoth D, Koch M, Keck CM. Terahertz-spectroscopy for non-destructive determination of crystallinity of L-tartaric acid in smartFilms® and tablets made from paper. Int. J. Pharm. 2020, 581, 119253, doi:10.1016/j.ijpharm.2020.119253.

[22] Ornik J, Heidrich L, Schesny R, Castro-Camus E, Keck CM, Koch M. Non-destructive crystallinity assessment of indomethacin in tablets made from smartFilms® using terahertz time-domain spectroscopy. Sci. Rep. 2022, 12, 1–7, doi:10.1038/s41598-022- 10041-1.

[23] Subrahmanyeswari CD, Prasanth Y, Sameeda R. Formulation and development of efavirenz tablets by paper technique using co-solvency method. Int. J. Curr. Pharm. Res. 2019, 11, 87–92, doi:10.22159/ijcpr.2019v11i6.36349.

[24] Sikarra D, Shukla V, Kharia AA, Chatterjee DP. Techniques for solubility enhancement of poorly soluble drugs: an overview, review article. J Med Pharm Allied Sci 2012;1:18-38.

[25] Parve B, Shinde P, Rawat S, Rathod S. Waghmode G. Solubility enhancement techniques: a review. World J Pharm Pharm Sci 2014;3:400-22.

[26] Kesharwani A, Kesharwani A, Maqbool MA. Solubilization enhancement techniques: an overview. Pharm Chem J 2017;4:121-30.