IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

Review of the Impact of Polymers on the Pharmaceutical Industry

KEHINDE ESTHER, AYODEJI

Abstract:
The impact of polymers on the pharmaceutical industry is the focus of this review. With the widespread use of complementary and alternative medicines, ensuring consistent access to medications poses a challenge, especially in low- and middle-income countries. However, the integration of polymers into drug delivery systems has facilitated local pharmaceutical production. This review examines the applications of polymers in areas such as polymeric therapeutics, drug delivery systems, biopharmaceutical manufacturing and processing aids, and primary packaging, with a focus on the Nigerian context. The review highlights recent trends and translational insights, opportunities and challenges associated with incorporating polymeric technologies, the importance of edible polymers in pharmaceutical progress, and diverse approaches in polymer drug delivery systems. Although there are challenges, such as cost, quality, and regulatory compliance, polymers have significant implications in pharmaceutical manufacturing and patient care, particularly in drug delivery, controlled release, and packaging. The future of polymer technology in the pharmaceutical industry relies on ongoing research and unlocking the full potential of polymers.

Keyword: Polymers, Pharmaceutical, Polymerization, Industry

1.0. Introduction

Complementary and alternative medicines (CAM), encompassing traditional treatments and practices, are estimated to be relied upon as a healthcare approach by approximately 80% of the global population, according to 2017 data from the World Health Organization (WHO). This widespread reliance, especially prominent in low- and middle-income countries, persists amidst the significant challenge of ensuring consistent access to conventional medicines in these regions. A review by Li et al. (2020) found that in many African countries, up to 90% of the population utilizes traditional medicine as a primary source of healthcare and treatment.

In light of these healthcare access barriers, domestic pharmaceutical production has gained increasing prominence in improving availability and affordability of essential medicines in Africa and Asia (WHO, 2011). To enable scale-up of local drug manufacturing, adoption of scientific and technological innovations is imperative. As highlighted by Ngwuluka et al. (2014), biopolymers have emerged as "high-impact pharmaceutical excipients," offering advantages such as renewable sourcing, biodegradability and low eco-toxicity. Accordingly, in 2019 the Nigerian National Agency for Food and Drug Administration and Control (NAFDAC) introduced new legislation and initiatives promoting development of the indigenous pharmaceutical industry.

Integral to optimizing pharmaceutical research and manufacturing processes, polymeric materials enable modulation of factors such as drug solubility, release characteristics and bioavailability in order to improve

therapeutic outcomes (Srivastava, 2016). Concurrently, pharmaceutical packaging has become an increasingly complex undertaking, with growing regulatory emphasis on principles of quality-by-design and rigorous scientific validation (Yoshida, 2019). As highlighted in a review by Lyashenko et al. (2018), specialty polymers and "smart" polymeric containers are playing a pivotal role in ensuring quality, safety and efficacy of formulations through the supply chain.

This comprehensive review aims to analyze the evolving impact of polymeric materials on the advancement of the pharmaceutical industry, focusing specifically on the Nigerian context as a representative emerging market. We examine applications spanning areas such as polymeric therapeutics, drug delivery systems, biopharmaceutical manufacturing and processing aids, as well as primary packaging. The present examination elucidates the diverse chemical nature of polymers typically employed in pharmaceuticals, while highlighting examples from the literature underscoring recent trends and translational insights. Lastly, we discuss opportunities and challenges associated with further integration of polymeric technologies for promoting growth of the domestic drug manufacturing sector.

2.0. Polymer and Their Evolution in Medicine

Polymers have played a significant role in the evolution of medicine, with their utilization dating back to ancient civilizations. The term "polymer" signifies "many parts," denoting large molecules composed of numerous repeating units called mers (Charles and Carraher, 2003). Over the centuries, polymers have been classified into various categories based on their properties and applications (Charkraborty, 2019). Today, they are indispensable in modern medicine, with applications ranging from drug delivery systems to tissue engineering and regenerative medicine.

The ancient roots of polymers in medicine extend over four millennia. Ancient papyrus papers from 4000 B.C. documented their use in sutures and wound closure, showcasing an early recognition of their medical applications (Veigas, 2009 & Metwaly et al., 2021). This early utilization of polymers demonstrated the understanding of their beneficial properties, such as their mechanical strength and compatibility with biological systems. These properties continue to be highly valued in medical applications today.

Around 2000 B.C., early practitioners explored the use of metals for bone repair, marking a significant milestone in medical history. The use of metals in medical applications continued to evolve over time and remains an important aspect of modern orthopedics. Metal implants and prostheses have revolutionized the field of joint replacement surgery, allowing patients to regain mobility and improve their quality of life.

According to Jin et al. (2017), goose quills were later employed for vascular repair, demonstrating the innovative spirit of medical pioneers. The use of natural polymers, such as quills, showed promise for restoring the functionality of blood vessels. However, it was not until the 1800s that metals played a crucial role in bone reconstruction. The development of metal plates, screws, and nails provided stability and support to fractured bones, facilitating the healing process.

Meanwhile, western medicine was not formally introduced into Nigeria until the 1860s, when the Sacred Heart Hospital was established by Roman Catholic missionaries in Abeokuta which also played a major role in the supply of modern health care facilities in Nigeria (Photius, 2020).

The 1930s saw the advent of synthetic polymers, coinciding with the growth of the plastic industry and presenting novel possibilities in medical applications (Vallejos et al., 2022). The development of synthetic polymers opened up a whole new realm of biomaterials with tailored properties for specific medical needs. These polymers could be precisely engineered to have the desired mechanical, chemical, and biological characteristics, making them versatile for various applications in medicine.

The post-World War II era, characterized by a pressing need for innovative medical devices due to heavy casualties, became a catalyst for advancements in biomaterials and the announcement of a ten-year development plan for the Nigerian health sector (Photius, 2020). Materials initially designed for industrial purposes, such as cellophane sausage casings, paved the way for groundbreaking developments in medicine. One such example is Dr. Kolff's artificial kidney, which was made possible by utilizing a polymer-based membrane to mimic the function of a natural kidney (Haas, 1952; Voinova et al., 2019).

Dr. Scribner's work with arteriovenous (A/V) shunts in 1960 was made possible by the availability of polymers like polysiloxane and polytetrafluoroethylene (Rezvova et. al., 2023). These polymers provided the necessary biocompatibility, flexibility, and durability for the construction of A/V shunts, which revolutionized dialysis treatment for patients with end-stage renal disease.

Polymers, with their transformative potential, continued to revolutionize medicine in the following decades. According to Elijah et al., (2013) they transitioned from early vascular grafts using polymethyl methacrylate to the widespread use of synthetic polymer fabrics. Dacron, a specially woven and knitted tubular fabric, became a staple in large artery repair (Improve Life, 2017). The development and refinement of polymer-based stents have revolutionized the treatment of cardiovascular diseases, providing a minimally invasive alternative to traditional surgical procedures.

In recent years, advances in polymer science and engineering have paved the way for even more innovative medical applications. Polymer-based drug delivery systems have allowed for targeted and controlled release of medications, improving treatment efficacy while minimizing side effects (Thamilselvan et. al., 2023). The field of tissue engineering has also greatly benefited from polymers, with scaffolds and matrices providing support and structure for the regeneration of damaged tissues.

Furthermore, the utilization of biodegradable polymers has brought about significant breakthroughs in the development of bioresorbable implants. These implants can be gradually absorbed by the body over time, eliminating the need for surgical removal and reducing the risk of complications. This has particularly revolutionized orthopedic surgery, where bioresorbable implants can be used for fracture fixation and bone regeneration (Wang et al., 2023).

Polymers offer several advantages in medical applications, making them highly desirable in the field of healthcare. They provide cost-effectiveness and tailorable molecular weights for diverse applications. By blending different polymers together, customized materials with superior properties can be created, which are unachievable from individual components (Pillay et al., 2013). For example, combining polystyrene with polybutadiene results in a material with enhanced impact resistance.

The utilization of polymers in medicine has come a long way since ancient civilizations. From early applications in wound closure and bone repair to the modern development of complex drug delivery systems and tissue regeneration techniques, polymers have continuously pushed the boundaries of medical advancements. Thanks to ongoing innovations and discoveries in polymer science, the potential for polymers in medicine is limitless.

In conclusion, the continual evolution of biomaterials offers new possibilities for personalized medicine and transformative treatments that bridge ancient practices with cutting-edge technologies. Polymers have not only transformed the field of medicine but also significantly improved the quality of life for countless patients worldwide. With further research and development, the potential for polymers to revolutionize medicine and contribute to advancements in healthcare is boundless.

3.0. Classification of Polymers in Pharmaceuticals

Polymers are widely used in the pharmaceutical industry due to their unique chemical and physical properties that make them well suited for use in various applications. The classification of polymers in pharmaceuticals can be broadly divided into three categories - conventional dosage forms, controlled release dosage forms, and packaging. Each of these categories has numerous applications where polymers play a crucial role in delivering effective and safe healthcare products to the consumers.

3.1. Polymers in Conventional Dosage Forms

One crucial application of polymers in the pharmaceutical industry is in conventional dosage forms. Conventional dosage forms refer to the typical forms used in drug delivery, such as tablets, capsules, granules, and powders. Polymers are used in these forms as binders, diluents, disintegrants, and coatings. This is further discussed below:

1. Binders: Polymers play a crucial role as binders in conventional dosage forms. Binders are materials that hold together the constituents of a formulation, allowing the tablet or capsule to be compressed or molded into a solid form. The most commonly used binders in the pharmaceutical industry are polyvinylpyrrolidone (PVP), hydroxypropyl cellulose (HPC), and hydroxyethyl cellulose (HEC) (Lachman et al., 1986).
Furthermore, PVP is a water-soluble polymer that is highly effective in ensuring the cohesiveness of tablets. It is commonly used in tablet formulations due to its excellent binding properties, compatibility with active ingredients, and low cost. HPC and HEC are also frequently used as binders in tablets and other conventional dosage forms. They are water-soluble cellulose derivatives that are useful in forming robust tablets while providing excellent disintegration properties (Kurakula & Rao, 2020).

2. Diluents: According to the United States Pharmacopeial Convention, (1979) diluents are excipients used in conventional dosage forms to increase tablet size, ensure homogenous drug distribution, and achieve uniformity in dosage. The most commonly used polymers as diluents are microcrystalline cellulose (MCC), lactose, and dextran (Rahman, 2020). MCC, a highly purified cellulose obtained from wood pulp, is an excellent diluent due to its high bulk density, good flow properties, and compressibility. It provides good disintegration and dissolution properties, making it useful in conventional dosage forms such as tablets and capsules. Lactose, derived from milk sugar, is also a commonly used diluent. It has minimal effect on tablet hardness and dissolution, and it is especially useful in low-dose tablets and chewable formulations. Dextran, a water-soluble polymer, is useful in the manufacture of sustained-release tablets, and it increases the solubility and bioavailability of poorly soluble drugs (Yohana et al., 2020).

3. Disintegrants: Disintegrants are materials added to conventional dosage forms to facilitate the breakup of tablets or capsules into small particles and release of the active ingredient(s) for absorption. Commonly used disintegrants include cross-linked polyvinylpyrrolidone (PVPXL), sodium starch glycolate (SSG), and croscarmellose sodium (Markl, 2017). PVPXL is a cross-linked form of PVP, making it more resistant to moisture and other environmental factors. It is commonly used in rapidly disintegrating tablets, providing excellent disintegration properties and quick drug release. SSG, a water-soluble starch, is highly effective in promoting the rapid disintegration of tablets and is used as a disintegrant and a suspending agent. Croscarmellose sodium, a water-soluble polymer, is widely used as a disintegrant due to its excellent water absorption capacity. It swells rapidly in the presence of water, causing the tablet to break apart and allowing the release of active ingredients (Rudnic et al., 1982).

4. Coatings: Coatings are layers applied to tablets to protect the active ingredient from environmental factors and gastric fluids and improve the aesthetic appeal of the tablet. There are several types of coatings, including film coatings, sugar coatings, and enteric coatings. Polymers that are commonly used as coatings include ethyl cellulose, hydroxypropyl methylcellulose (HPMC), and Eudragit (Aulton, 2007).
Ethyl cellulose is a water-insoluble polymer that provides high resistance to moisture and is ideal for use in enteric coatings (Rekhi, & Jambhekar, 2008). HPMC, another cellulose derivative, is used in the development of conventional dosage forms due to its excellent release-modifying properties. It is useful in enteric and sustained-release coatings. Eudragit is a family of acrylic polymers designed for film coatings, enteric coatings, and

sustained release formulations. They provide excellent protection to the active ingredients and resist gastric acids, leading to improved bioavailability and patient compliance.

From the foregoing, the properties, such as small size, uniformity, and reproducibility make them ideal binders, diluents, disintegrants, and coatings. Polymers used in conventional dosage forms must meet specific criteria to ensure stability, efficacy, bioavailability, and ease of administration. Continued research and improvements in polymer science promise even more efficient, effective, and sustainable ways to develop and improve upon existing conventional dosage forms (Adepu and Ramakrishna, 2021)

3.2. Polymers in Controlled Release Dosage Forms

Controlled release dosage forms refer to pharmaceutical formulations that release therapeutic agents into the body at a predetermined rate and for a specific duration. These formulations provide a sustained and targeted therapeutic effect, reducing the number of doses required and minimizing adverse side effects. The use of polymers in controlled release dosage forms is critical as they help regulate and control the rate and extent of drug release, ensuring optimal therapeutic outcomes (Liechty et al., 2010). Polymers in controlled release dosage forms are classified into two categories – non-degradable and degradable polymers. Non-degradable polymers form a physical barrier around the drug to control its release, while degradable polymers break down over time, releasing the drug. This is further explicit below:

a. **Non-Degradable Polymers:** Non-degradable polymers, such as ethyl cellulose (EC) and cellulose acetate phthalate (CAP), are widely used to provide sustained drug release by forming a physical barrier around the drug, which controls its release over time (Adeleke, 2019). These polymers are particularly useful for water-insoluble drugs or drugs with low solubility in water, as they provide a slow, sustained release of the drug over an extended period.

   Ethyl cellulose is a commonly used non-degradable polymer due to its low toxicity, excellent biocompatibility, and compatibility with a wide range of drugs. Ethyl cellulose-based formulations are available in tablet and capsule forms and are used to provide controlled release of drugs, such as anti-inflammatory agents, anti-cancer drugs, and cardiovascular drugs (Dow, 2016).

   Cellulose acetate phthalate is another widely used non-degradable polymer in controlled release dosage forms. It is particularly useful for drugs that are sensitive to changes in pH levels, as it provides a controlled release by swelling in an acidic environment and contracting in an alkaline environment. Cellulose acetate phthalate-based formulations are used to provide sustained release of drugs, such as anti-inflammatory agents and analgesics.

b. **Degradable Polymers:** Degradable polymers, on the other hand, are designed to break down over time and release the drug. These polymers can be further classified into two subcategories - hydrophilic and hydrophobic polymers (Siepmann and Peppas, 2001). Hydrophilic polymers absorb water and form a gel-like matrix that swells and releases the drug. Conversely, hydrophobic polymers degrade over time, releasing the drug slowly as they break down in the body. Degradable polymers are particularly useful for sustained drug release and targeted drug delivery applications.

   i. **Hydrophilic Polymers:** Hydrophilic polymers, such as polyvinyl alcohol (PVA) and hydroxypropyl methylcellulose (HPMC), are water-soluble polymers that form a gel-like matrix when exposed to water (Hirun & Kraisit, 2022). These polymers are used to provide a slow release of drugs and are particularly useful for the controlled release of water-soluble drugs.

   Polyvinyl alcohol-based formulations are available in tablet and capsule forms and are used to provide sustained release of drugs, such as anti-cancer agents and anti-inflammatory drugs.

Hydroxypropyl methylcellulose-based formulations are commonly used as a film-coating material for tablets and capsules (ECHEMI, 2023). The hydrophilic nature of this polymer imparts excellent adhesion and film-forming properties, providing a sustained release of the drug.

ii. **Hydrophobic Polymers:** Hydrophobic polymers, such as polylactide-co-glycolide (PLGA) and poly(lactic acid) (PLA), are biodegradable polymers that slowly release the drug as they break down in the body (Makadia & Siegel, 2011). These polymers are particularly useful for sustained drug release and targeted drug delivery applications and have been extensively studied in the field of drug delivery.

PLGA- and PLA-based formulations are available in various forms, including microspheres, nanoparticles, and implants (Jain, 2000). These polymers are used to provide sustained release of drugs over an extended period and are particularly useful for delivering lipo-soluble drugs.

PLGA-based formulations are widely used in the targeted delivery of anti-cancer drugs. The biodegradation of PLGA results in the sustained release of the drug, thus providing a higher concentration of the drug at the target site for a more extended period (Makadia & Siegel, 2011). Additionally, PLGA-based formulations are also used in the delivery of vaccines and gene therapy as they can provide sustained release of antigens or gene vectors, resulting in a prolonged immune response or gene expression.

In conclusion, polymers play a crucial role in controlled release dosage forms, providing sustained and targeted therapeutic outcomes. Non-degradable polymers, such as ethyl cellulose and cellulose acetate phthalate, form a physical barrier around the drug, which controls its release over time. Degradable polymers, on the other hand, release the drug slowly as they break down in the body. Hydrophilic polymers, such as PVA and HPMC, are useful for the controlled release of water-soluble drugs, while hydrophobic polymers, such as PLGA and PLA, are useful for sustained drug release and targeted drug delivery applications.

Ongoing research in the field of polymer science will likely lead to further innovations in the use of polymers in controlled release dosage forms, promising more effective, efficient, and safe healthcare products for patients around the world.

3.3 Polymers for Packaging

Polymers are widely used in the packaging industry due to their unique properties such as flexibility, durability, and resistance to chemical and environmental factors (Pechyen and Srichana, 2013). The use of polymers in packaging offers several benefits such as reduced product contamination, increased shelf-life, and improved aesthetics (Jamróz et al., 2018). The different types of polymers used in packaging and their unique properties and applications are discussed below:

Table 1: Types of Polymers Used in Packaging and Their Characteristics and Applications

Type of Polymer	Chemical Formula	**Type of Polymer**	**Characteristics**	**Common Applications**
Polyethylene (PE)	$(C_2H_4)_n$	High-Density Polyethylene (HDPE) Low-Density Polyethylene (LDPE) Linear Low-Density Polyethylene (LLDPE)	Excellent strength, durability, and resistance to heat, chemicals, and water	Bottles, bags, containers, shrink wrap, pharmaceutical packaging
Polypropylene (PP)	$(C_3H_6)_n$	Homo-polymer polypropylene (PP-H), Block-Copolymer polypropylene (PP-B), and Random-Copolymer polypropylene (PP-R)	Excellent strength-to-weight ratio, durability, and resistance to heat, moisture, and chemicals	Bottles, containers, packaging film, pharmaceutical packaging
Polystyrene (PS)	$(C_8H_8)_n$	Expanded Polystyrene (EPS) Crystal Polystyrene (CPS)	Rigidity, clarity, and ease of processing	Packaging food products, electronics,

				pharmaceutical packaging
Polyethylene terephthalate (PET)	$(C_{10}H_8O_4)_n$	Virgin PET, Recycled PET (rPET), Amorphous PET (APET) and Glycol-modified PET (PETG)	Excellent barrier properties, durability, and transparency	Bottles, jars, trays, pharmaceutical packaging
Polyvinyl chloride (PVC)	$(C_2H_3Cl)_n$	Unplasticized PVC (uPVC), Plasticized PVC (pPVC), Chlorinated PVC (CPVC), Foam PVC and Biocompatible PVC	Excellent chemical resistance, durability, and flexibility	Bottles, blister packaging, shrink wrap, pharmaceutical packaging
Polycarbonate (PC)	$(C_{15}H_{16}O_2)_n$	General Purpose Polycarbonate, Flame Retardant Polycarbonate, Optical Glass Polycarbonate, Recycled Polycarbonate and UV Resistant Polycarbonate	Excellent impact resistance, transparency, and durability	CD/DVD cases, eyeglasses, medical devices, pharmaceutical packaging
Polyamide (PA)	[(NH-(CH_2)5-CO)x]n	(Nylon 6 or Nylon 6/6)	Excellent strength, durability, and resistance to heat and chemicals	Tubes, bags, films, pharmaceutical packaging

Generally, the selection of a polymer for packaging depends on several factors such as the application, product requirements, and environmental concerns. The variability in polymer properties and characteristics has allowed for the development of new and innovative packaging solutions that cater to specific needs. As concerns about environmental sustainability continue to grow, the development of biodegradable polymers and incorporating recycling and reuse into packaging design will continue to play an essential role in the pharmaceutical industry.

4.0. Conclusion:

To summarize, the use of polymers has had a significant impact on the pharmaceutical industry, dating back to ancient civilizations. Polymers possess unique properties that make them well-suited for various pharmaceutical applications. They are widely used in conventional dosage forms as binders, diluents, disintegrants, and coatings, enhancing the structural integrity, homogeneity, and controlled release of active ingredients. In controlled release dosage forms, both non-degradable and degradable polymers are crucial in regulating the rate and extent of drug release, providing optimal therapeutic outcomes. Additionally, polymers are extensively used in packaging due to their flexibility, durability, and resistance to chemical and environmental factors. The utilization of polymers in the pharmaceutical industry enhances drug delivery, stability, and safety. Advances in polymer science offer potential for further innovations and applications in the pharmaceutical field.

References

Adeleke O. A. (2019). Premium ethylcellulose polymer based architectures at work in drug delivery. International journal of pharmaceutics: X, 1, 100023. https://doi.org/10.1016/j.ijpx.2019.100023

Aulton, M. E. (2007). Pharmaceutics: The Science of Dosage Form Design (2nd ed.). Churchill Livingstone.

Charles, E. and Carraher, Jr. (2003). Polymer Chemistry. Marcel Dekker, New York

Dow, (2016). Ethocel™ Ethylcellulose – A technical review. Retrieved from http://msdssearch.dow.com/PublishedLiteratureDOWCOM/dh_08e5/0901b803808e5465.pdf?filepath=dowwolff/pdfs/noreg/198-02293.pdf&fromPage=GetDoc

ECHEMI. (2023). Major HPMC Uses in Pharmaceuticals Introduced. Retrieved from https://www.echemi.com/cms/1418811.html

Elijah I. Nep, Patricia O. Odumosu, Ndidi C. Ngwuluka, Patrick O. Olorunfemi, Nelson A. Ochekpe, "Pharmaceutical Properties and Applications of a Natural Polymer from Grewia mollis", Journal of Polymers, vol. 2013, Article ID 938726, 8 pages, 2013. https://doi.org/10.1155/2013/938726

Haas, G. (1952). Über die künstliche Niere. DMW-Deutsche Medizinische Wochenschrift, 77(52), 1640-1641.

Hirun, N., & Kraisit, P. (2022). Drug-Polymers Composite Matrix Tablets: Effect of Hydroxypropyl Methylcellulose (HPMC) K-Series on Porosity, Compatibility, and Release Behavior of the Tablet Containing a BCS Class I Drug. Polymers, 14(16), 3406. https://doi.org/10.3390/polym14163406

Improve Life, (2017). Synthetic Polymers & Tissue Adhesives. Veterinary Surgery Online, University of Guelph. Retrieved from https://www.vetsurgeryonline.com/synthetic-polymers-tissue-adhesives/

Jain, R. A. (2000). The manufacturing techniques of various drug loaded biodegradable poly(lactide-co-glycolide) (PLGA) devices. Biomaterials, 21(23), 2475-2490. https://doi.org/10.1016/S0142-9612(00)00115-0

Jamróz, W., Kurek, M., Łyszczarz, E., & Jachowicz, R. (2018). Modern pharmaceutical packaging: From fundamentals to innovative techniques. International Journal of Pharmaceutics, 544(2), 325-342. https://doi.org/10.1016/j.ijpharm.2018.04.060

Jin E., Reddy N., Zhifeng Z., and Yang Y., (2017). Graft Polymerization of Native Chicken Feathers for Thermoplastic Applications. Journal of Agricultural and Food Chemistry. 59(5):1729-38

Kurakula, M., & Rao, G. S. N. K. (2020). Pharmaceutical assessment of polyvinylpyrrolidone (PVP): As excipient from conventional to controlled delivery systems with a spotlight on COVID-19 inhibition. Journal of drug delivery science and technology, 60, 102046. https://doi.org/10.1016/j.jddst.2020.102046

Lachman, L., Lieberman, H. A., & Kanig, J. L. (1986). The Theory and Practice of Industrial Pharmacy (3rd ed.). Lea & Febiger.

Li, S., Odedina, S., Agwai, I., Ojengbede, O., Huo, D., & Olopade, O. I. (2020). Traditional medicine usage among adult women in Ibadan, Nigeria: a cross-sectional study. BMC complementary medicine and therapies, 20(1), 93. https://doi.org/10.1186/s12906-020-02881-z

Liechty, W. B., Kryscio, D. R., Slaughter, B. V., & Peppas, N. A. (2010). Polymers for drug delivery systems. Annual review of chemical and biomolecular engineering, 1, 149–173. https://doi.org/10.1146/annurev-chembioeng-073009-100847.

Lyashenko, V., Sotnik, S., & Babker, A. M. A. (2018). Features of Packaging from Polymers in Pharmaceutics. Saudi Journal of Medical and Pharmaceutical Sciences, 4(2), 166-174.

Makadia, H. K., & Siegel, S. J. (2011). Poly Lactic-co-Glycolic Acid (PLGA) as Biodegradable Controlled Drug Delivery Carrier. Polymers, 3(3), 1377–1397. https://doi.org/10.3390/polym3031377

Markl, D., & Zeitler, J. A. (2017). A Review of Disintegration Mechanisms and Measurement Techniques. Pharmaceutical research, 34(5), 890–917. https://doi.org/10.1007/s11095-017-2129-z.

Metwaly, A. M., Ghoneim, M. M., Eissa, I. H., Elsehemy, I. A., Mostafa, A. E., Hegazy, M. M., Afifi, W. M., & Dou, D. (2021). Traditional ancient Egyptian medicine: A review. Saudi journal of biological sciences, 28(10), 5823–5832. https://doi.org/10.1016/j.sjbs.2021.06.044

National Agency for Food and Drug Administration and Control, (2019). Five plus five-year validity (migration to local production). Abuja, Nigeria. Available from: https://www.nafdac.gov.ng/five-plus-five-year-validity-migration-to-local-production-03191/

Ngwuluka, N., Ochekpe, N., & Aruoma, O. (2014). Naturapolyceutics: The Science of Utilizing Natural Polymers for Drug Delivery. Polymers, 6(5), 1312–1332. MDPI AG. Retrieved from http://dx.doi.org/10.3390/polym6051312

Pechyen, C., & Srichana, T. (2013). Pharmaceutical packaging materials. In S. S. J. Hsieh (Ed.), Development of new anticancer drugs (pp. 285-318). Springer. https://doi.org/10.1007/978-1-4614-7060-9_10

Photius. (2020). Nigeria History of Modern Medical Services. The Library of Congress Country Studies; CIA World Factbook. https://photius.com/countries/nigeria/society/nigeria_society_history_of_modern_me~10005.html#:~:text=Western%20medicine%20was%20not%20formally,health%20care%20facilities%20in%20Nigeria

Rahman, Z., Charoo, N. A., Kuttolamadom, M., Asadi, A., Khan, M. A., Faintuch, J., & Faintuch, S. (2020). Precision Medicine for Investigators, Practitioners and Providers. Academic Press, 473-481. https://doi.org/10.1016/B978-0-12-819178-1.00046-0

Rekhi, G. S., & Jambhekar, S. S. (2008). Ethylcellulose - A Polymer Review. Drug Development and Industrial Pharmacy, 21(1), 61-77. https://doi.org/10.3109/03639049509048096

Rezvova, M.A.; Klyshnikov, K.Y.; Gritskevich, A.A.; Ovcharenko, E.A. (2023). Polymeric Heart Valves Will Displace Mechanical and Tissue Heart Valves: A New Era for the Medical Devices. Int. J. Mol. Sci. 2023, 24, 3963. https://doi.org/10.3390/ijms24043963

Rudnic, E. M., Rhodes, C. T., Welch, S., & Bernardo, P. (1982). Evaluations of the mechanism of disintegrant action. Drug Development and industrial pharmacy, 8(1), 87-109.

Siepmann, J., & Peppas, N. A. (2001). Modeling of drug release from delivery systems based on hydroxypropyl methylcellulose (HPMC). Advanced Drug Delivery Reviews, 48(2-3), 139-157. https://doi.org/10.1016/S0169-409X(01)00112-0

Srivastava, A., Yadav, T., Sharma, S., Nayak, A., Kumari, A., & Mishra, N. (2016). Polymers in Drug Delivery. Journal of Biosciences and Medicines, 4(1),

Thamilselvan, G., David, H., Sajeevan, A., (2023). Polymer based dual drug delivery system for targeted treatment of fluoroquinolone resistant Staphylococcus aureus mediated infections. Sci Rep 13, 11373 (2023). https://doi.org/10.1038/s41598-023-38473-3

United States Pharmacopeial Convention, Inc. (1979). The United States Pharmacopeia. The National Formulary. Rockville, MD.

Vallejos, S., Trigo-López, M., Arnaiz, A., Miguel, Á., Muñoz, A., Mendía, A., & García, J. M. (2022). From Classical to Advanced Use of Polymers in Food and Beverage Applications. Polymers, 14(22), 4954. https://doi.org/10.3390/polym14224954

Veiga, P., (2009). Health and Medicine in ancient Egypt; magic and science.

Voinova, M., Repin, N., Sokol, E., Tkachuk, B., & Gorelik, L. (2019). Physical Processes in Polymeric Filters Used for Dialysis. Polymers, 11(3), 389. MDPI AG. Retrieved from http://dx.doi.org/10.3390/polym11030389

Wang, P., Gong, Y., Zhou, G., Ren, W., & Wang, X. (2023). Biodegradable Implants for Internal Fixation of Fractures and Accelerated Bone Regeneration. *ACS Omega, 8*(31), 27920-27931. https://doi.org/10.1021/acsomega.3c02727

World Health Organization, (2011). Local production for access to medical products: developing a framework to improve public health. Geneva: World Health Organization; 2011. Available from: https://www.who.int/phi/publications/local_production_policy_framework/en/

Yohana Chaerunisaa, A., Sriwidodo, S., & Abdassah, M. (2020). Microcrystalline Cellulose as Pharmaceutical Excipient. IntechOpen. doi: 10.5772/intechopen.88092