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QUALIFICATION WORK

on the topic: «**INVESTIGATION OF SACHET PACKAGING MATERIAL INFLUENCE ON THE TERM OF STORAGE OF ECTAMPORANEOUS POWDERS**»

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ANNOTATION

The qualification work is devoted to to research on the influence of sachet packaging material on the shelf life of pharmacy powders.

The qualification work is set out on 62 pages of typewritten text, consists of an introduction, three chapters, general conclusions and a list of references. The bibliography contains 38 sources. The work is illustrated with 5 tables and 10 figures.

Key words: powder, technology, sachets, packaging material, shelf life.

АНОТАЦІЯ

Кваліфікаційна робота присвячена дослідженням з вивчення впливу пакувального матеріалу саше на термін зберігання порошків аптечного виробництва.

Кваліфікаційна робота викладена на 62 сторінках машинописного тексту, складається зі вступу, трьох розділів, загальних висновків, списку використаних літературних джерел. Список літератури містить 38 джерел. Робота ілюстрована $5^{\text{ма}}$ таблицями та $10^{\text{ма}}$ рисунками.

Ключові слова: порошок, технологія, саше, пакувальний матеріал, термін зберігання.

CONTENTS

INTRODUCTION

Actuality of the topic. A sachet is a flat three-seam or four-seam package used to store medicines and dietary supplements. The name of the package comes from the French word "sachet" (bag). The design involves the use of multi-layer polymer films or combined materials with increased tightness and high barrier properties. Thanks to these properties, the sachet perfectly preserves and protects the packaged product during the stated shelf life.

Sachet-type packaging is used in the food, pharmaceutical, chemical and other industries and is used for portion packaging of products of various consistency: loose, liquids, gels, creams, paste-like preparations.

Packaging material for pharmaceutical powders significantly affects the shelf life and ensuring the stability of the product from the moment of manufacture to the last day of storage. It is extremely important to choose the right material, taking into account the physical and chemical properties of the ingredients that make up the powder.

In recent years, the variety of types of packaging material allows you to choose the one that best meets the requirements of a specific composition of powders. It is possible to choose packaging from classic paper to modern multi-layer sachets.

Therefore, research on the influence of packaging material and the stability and shelf life of powders is an urgent and timely task of modern pharmacy.

The aim of our work is to study the influence of the type of sachet packaging material on the stability and shelf life of pharmaceutical powders.

Tasks of the study

To achieve the aim, the following tasks were set:

- analyze data from scientific literature regarding the stages of development of solid dosage forms and materials for their packaging;
- to analyze the range of medicinal products entering the pharmaceutical market of the country in the medicinal form of sachets;

- conduct a comparative analysis of the quality of API-based powders with different physical and chemical properties during storage for 6 months;
- to establish the material of the sachet, which is the most promising for packing powders of extemporaneous production.

Object of study. Pharmaceutical study of the influence of packaging material on the stability and shelf life of pharmaceutical powders.

Subject of study. Study of the influence of the type of packaging material "sachet" on the stability and shelf life of pharmacy powders.

Methods of research. Bibliosemantic, well-known organoleptic (appearance, color, smell), physico-chemical (average mass and deviation in mass, identification and quantification), organizational-economic and mathematical (statistical processing of results) methods were used to solve the problems set in the qualification work. studies that allow to objectively evaluate the qualitative and quantitative indicators of the studied samples of powders in different sachets on the basis of experimentally obtained and statistically processed results.

Practical significance of the obtained results. The results of the study of the quality of powders with active pharmaceutical ingredients (APIs) of various physicochemical properties, which were stored in sachets made of materials of different quality, are given, which will allow to expand the assortment of sachets used in pharmacy production for packaging extemporaneous powders.

Implementation of results and publication. The results of the work were discussed within the framework of scientific seminars and meetings of the SSS of the pharmaceutical technology of drugs department.

Structure and scope of qualification work.

The qualification work is set out on 62 pages of typewritten text, consists of an introduction, three chapters, general conclusions and a list of references. The bibliography contains 38 sources. The work is illustrated with 5 tables and 10 figures.

CHAPTER 1

HISTORY OF POWDERS AS DOSAGE FORM. TYPES OF PACKAGING

1.1. History Of Solid Dosage Forms

The origins of medicinal powders trace back to ancient civilizations, where primitive practices of herbal medicine prevailed, the earliest recorded use of powders as a dosage form can be traced back to ancient Egypt, where they were used for medicinal purposes. Recognizing the therapeutic potential of various plant parts such as leaves, stems, roots, barks, and berries, likely consumed them internally to alleviate a range of ailments [2].

Powders, known as "herb simples," were often prepared by grinding herbs, minerals, and other natural substances into a fine consistency, which could then be mixed with water or other liquids for consumption. This method of preparation allowed for a high degree of customization, as the ingredients and proportions could be adjusted to suit the individual needs of each patient. involved methods such as chewing roots and barks, and applying leaves externally with animal fats to treat wounds and abrasions.

Additionally, inhalation therapy likely emerged, with individuals placing herbs on fires to inhale the resultant vapors for medicinal benefits. As medical knowledge progressed, herbal combinations were formulated, often incorporating materials like fats, oils, and honey. Over time, these natural substances underwent processing to enhance their efficacy and palatability. Techniques such as boiling to extract medicinal properties, dissolution in solvents, grinding, and dilution with other substances became commonplace[2].

Moreover, efforts were made to improve the sensory aspects of these formulations; sweeteners were added to enhance taste, aromatic agents to improve odor, and dyes to enhance appearance. These refinements culminated in the development of diverse dosage forms, suitable for oral ingestion, topical application, or insertion into bodily orifices. This chapter delves into the historical evolution of such dosage forms, both internally and externally administered, in the quest to alleviate the physical afflictions of humanity[2].

Greek and Roman medicines:

In ancient Greece, the famous physician Hippocrates also recognized the benefits of powders as a dosage form. He prescribed various powdered remedies for a wide range of ailments, from digestive issues to respiratory problems. The use of powders continued to evolve throughout the Middle Ages, as new substances and techniques were discovered. Throughout the classical era, a diverse array of dosage forms was employed, ranging from ointments, oils, powders, pills, suppositories, gargles, to eye lotions. Enemas, alternatively referred to as clysters or glysters, represented a method of administering liquids into the rectum, facilitated by a horn or an animal bladder attached to a greased tube for insertion into the anus[2] [24] **.**

To alleviate discomfort, hot fomentations, such as sponges soaked in hot water or bran boiled in diluted vinegar and enclosed in a bladder, or toasted millet within a woolen cloth, were commonly applied. Cerates, comprising a mixture of oil, wax, and medicinal ingredients, served as external applications, distinguished by their firmness compared to poultices, which were similar dressings utilized to retain heat in affected areas[24].

Therapeutic practices of the time encompassed the use of minerals, herbs, and animal derivatives, with a notable example being a mineral-rich clay discovered on islands like Lemnos, fashioned into discs known as terra sigillata or sealed earth, indicative of their place of origin. Among the most significant medicinal formulations were treacles or theriacs, initially employed for the treatment of venomous bites or stings but later recognized as universal antidotes. These preparations, often comprising a multitude of ingredients, including honey, persisted in use well into the 19th century.

Roman physician Scribonius Largus, who accompanied the legions of Augustus to Britain, prescribed remedies containing chemical, animal, and herbal constituents. Such therapies were likely accessible to prominent citizens in larger cities and towns, as well as utilized by the military. However, ordinary individuals primarily relied on herbal remedies for their healthcare needs[27].

Medieval medicines

Following the withdrawal of the Romans in the early 5th century, three primary forms of medicine emerged in Britain: household and herbal medicine, monastic medicine rooted in classical texts and prayers, and the practice of Anglo-Saxon healers, known as leeches. Many of the texts produced by the latter group were compiled in manuscripts referred to as leech books[28].

In medieval times, the use of powders as a dosage form for medicines was prevalent, reflecting a historical practice that dates back centuries. Medicinal powders were often prepared by grinding herbs, minerals, and other natural substances into a fine consistency, allowing for easy administration. These powders were sometimes mixed with water or other liquids for consumption. To mask the often-unpleasant taste of certain powders, innovative solutions like cachets were developed. Cachets were rice-paper wafers that could enclose powders, making them easier to swallow by dipping them in water before ingestion[28] [29].

The process of preparing powders in medieval times involved weighing and mixing ingredients meticulously. Bulk powders were packed in containers like paper bags, glass, or tin, while individual doses were wrapped in quality paper. To prevent reactions between different powders, ingredients were often wrapped separately and mixed just before consumption[29].

Arab medicines

The use of powders as a dosage form in Arab medicine has a rich history, dating back to the early days of Arabic/Islamic civilization. The field of Arab medicine has made significant contributions to the development of pharmacy, with physicians exploring new drugs and writing about their therapeutic applications in booklets called "al-Mujarrabat". Early pharmacological development was influenced by the use of poison and antidote, with alchemists playing a crucial role in the field[2].

The Book on Poisons and Antidotes, written by the famous Arab alchemist Abu Musa Jabir ben Hayyan, is a seminal work that identifies poisons by their traits, natural origins, modes of action, dosages, methods of administration, and target organs, the later scientist and other Arab scientists, such as Yuhann ibn Masawayh and Hunayn bin Ishaq, have made significant contributions to the field of pharmacy and the understanding of medicinal plants, they have written about combining drugs and diets, arguing that the most successful physician is able to cure the disease only with a change of diet. They have also recommended using medicinal herbs to improve the body's natural resistance[16].

Two of the works attributed to Avicenna contain detailed instructions on the preparation of medicines, offering numerous formulae and a dedicated section on poisons. Avicenna is credited with introducing the practice of gilding and silvering pills, which added both aesthetic appeal and potentially therapeutic benefits to medications.

Arab pharmacists utilized sugar derived from sugar cane, initially cultivated in India and later propagated in regions including Persia, Cyprus, Sicily, and Spain. They notably introduced a variety of sweet preparations, including syrups, confections, and juleps.

Syrups were crafted by boiling a liquid with sugar, while conserves involved mixing flowers, herbs, roots, or fruits with sugar to preserve them. Confections, on the other hand, were concocted by blending dried and powdered ingredients with syrup or honey to achieve a consistency akin to a thin electuary. Although electuaries were denser than confections, they were susceptible to fermentation if too thin or candying if too thick. Juleps, characterized by their clarity and sweetness, served as pleasant vehicles for administering medicines[16].

In addition to sweeteners, Arab pharmacists incorporated flavors such as rose water, orange, and lemon to enhance the palatability of medicines. Their advancements in alchemy, which laid the foundation for modern chemistry, also facilitated the design of chemical apparatuses that would later influence European pharmaceutical practices during the early modern period[27].

Early modern medicine

The advent of the printing press in the illustrious mid-15th century heralded a profound transformation in the dissemination of medical wisdom, casting the veil of knowledge far and wide across the lands. Embodied within printed tomes, often penned in the revered tongue of Latin, lay the reservoirs of erudition accessible to scholars spanning distant realms. Noteworthy among these literary treasures was the Pharmacopeia Londinensis, unveiled in the annals of 1618, a pioneering opus that transcended provincial confines to encompass an entire nation - none other than the illustrious England herself, shunning the modest claims of city-states for the grandeur of a unified realm[29].

Yet, amidst the scholarly echelons, the lingua franca of Latin remained an elusive mistress, with but a scant few medical savants endowed with her grace. Thus, the blossoming proliferation of herbals, formularies, and dispensatories in the vernacular tongue of English ushered in an era of democratized enlightenment in the hallowed halls of medicine. For the very first time, the alchemical symphonies and elixirs of life could be deciphered in the common tongue, igniting a conflagration of understanding that swept through the hearts and minds of practitioners far and wide. These translations, exquisite in their craftsmanship, became cherished repositories of wisdom, offering glimpses into the diverse tapestry of medical tradition that adorned the 17th and 18th centuries[30].

Within the lush pages of these illuminated manuscripts lay not merely the humble herb simples, but a veritable cornucopia of medicinal marvels, drawn from the wellspring of ages past. Thus, the printed word, bedecked in the finery of English prose, emerged as a beacon of enlightenment, illuminating the path to healing for generations to come.

Powders were a common dosage form in early modern medicine, with various types of powders used for different purposes. For instance, purgative powder and boluses were used to purge the patient by evacuating their stomach and/or bowels, while astringent plasters were applied externally to provoke the contraction of skin or other bodily tissues. Stomachocephalic pills were prescribed to alleviate headaches and nausea, and Catholic powder was used as a general cure-all[17].

Powders were often mixed with other substances to create medicinal concoctions. For example, in the early modern period, a drink of wine mixed with garlic, crabs-eyes, and "the powder of a stag's pizzle" was used to treat bladder problems. Similarly, chestnuts were used to treat people coughing up blood due to their association with Jupiter, according to Nicholas Culpeper's 1652 work The English Physician.

The preparation of powders in early modern medicine was a complex process, with various methods used to ensure the correct dosage and administration. For instance, In the past, individuals would often consume disagreeable-tasting powders by wrapping them in a rice-paper wafer, which was softened by dipping in water before being swallowed along with a drink of water. This concept was expanded upon in France during the 1870s by Limousin of Paris, who introduced the cachet: two rice-paper cups joined together with powder enclosed inside[17]

History of medicinal powders technology behind it

The history of medical powders dates back to ancient times, where they were used as a convenient mode of administering drugs derived from hard vegetables such as roots, barks, and woods. With the introduction of synthetic drugs, Powders were traditionally employed to administer insoluble drugs like calomel, bismuth salts, mercury, and chalk. However, the swift advancement of formulations containing highly potent compounds has led to a decline in the use of powders as a dosage form, with tablets and capsules largely supplanting them[31].

Powders are characterized as dry, solid substances, comprising finely divided drugs with or without excipients, and designed for internal or external application. They represent a solid substance in finely divided form, typically acquired through processes such as crushing, grinding, or comminution.

The pharmaceutical uses of powders include administering insoluble drugs, setting liquid foundation/concealer so that the makeup lasts longer and does not move around, or rub off of your skin, and preparing powder formulation to understand hoppers and the process of transferring powders, methods of reducing particle size, and the diverse range of mills utilized[13].

The technology behind medical powders has evolved over time, with various types of powders being developed for different purposes. For instance, eutectic powders are made by mixing substances with low melting points, while efflorescent powders are made by mixing crystalline substances that liberate water of crystallization when present. These powders have specific uses and properties, such as low melting points or the ability to absorb moisture[22].

In the field of Additive Manufacturing (AM), metal powders are used in various manufacturing processes, such as Gas Atomization, Induction Melted Bar Atomization (EIGA), Plasma Atomized Wire (PAW), and Plasma Rotating Electrode Atomization (PREP). These processes involve disintegrating a molten metal stream into droplets using high-pressure gas or other methods, which then solidify before collection. The resulting metal powders have unique properties, such as high cleanliness and good flow rate, making them suitable for AM applications[25].

1.2 Evolution of Pharmacy containers

The evolution of pharmacy containers has been a fascinating journey that spans centuries, reflecting advancements in materials, technology, and the understanding of pharmaceutical packaging needs. From ancient civilizations to modern times, pharmacy containers have undergone significant transformations to meet the demands of storing and dispensing medications effectively. Let's delve into the detailed evolution of pharmacy containers

Ancient Times

Ancient civilizations recognized the importance of protecting and preserving medicines, leading to the development of various pharmacy containers. Clay pots, used in ancient Egypt, were an early form of pharmacy container that provided reliable storage and shielded medicines from environmental factors. These pots were often decorated with intricate designs, symbols, and inscriptions, indicating the contents and intended use of the stored substances[19].

Animal bladders, used in ancient Greece and Rome, served as pouches for liquid medications. They offered sturdiness and protection against evaporation, making them an ideal solution for transporting and storing liquid remedies. Glass bottles, also used by societies like Rome, were valued for their non-reactive nature, which helped preserve the medicinal properties of the stored substances. These early containers were sealed with corks or Natural stoppers were utilized to preserve the efficacy of the medications and prevent contamination[19].

The use of natural materials in ancient pharmacy containers reflected the resourcefulness and ingenuity of these early societies. The design and functionality of these containers were tailored to the specific needs of the medicines they stored, ensuring their effectiveness and safety. The use of seals and inscriptions on these containers added a layer of protection and identification, ensuring the authenticity and integrity of the stored substances[32].

In ancient Egypt, pharmacy containers were an essential part of medical practice. The Ebers Papyrus, an ancient Egyptian medical text, mentions various types of containers used for storing medicinal substances. These containers included clay pots, wooden boxes, and leather pouches. The use of seals and inscriptions on these containers was common, indicating the contents and the intended recipient of the stored substances[18].

In ancient Mesopotamia, pharmacy containers were used in the preparation and administration of medicines. The Assyrian medical texts, such as the Diagnostic Handbook of Esagil-kin-apli, describe the use of various types of containers for storing medicinal substances. These containers included clay pots, wooden boxes, and metal vessels. The use of seals and inscriptions on these containers was also prevalent, ensuring the authenticity and integrity of the stored substances[23].

In ancient China, pharmacy containers were an essential part of traditional Chinese medicine. The Huangdi Neijing, an ancient Chinese medical text, mentions various types of containers used for storing medicinal substances. These containers included bamboo tubes, ceramic jars, and silk pouches. The use of seals and inscriptions on these containers was common, indicating the contents and the intended use of the stored substances.

Classical Antiquity

During the classical period in Greece and Rome, pharmacy containers evolved to meet the growing demand for medicinal preparations. Glassmaking techniques advanced, leading to the production of glass bottles and vials for storing liquids and powders. These containers were often adorned with intricate designs and labels, showcasing the sophistication of ancient craftsmanship[6].

Glass containers were widely used in classical antiquity for storing medicines. The Greeks and Romans used lead and silver containers to hold medicines, while Byzantine silver pitchers were made of silver and brass. Prior to the adoption of tin-glazed ceramics, apothecaries are thought to have employed metal containers for storing medicines. During the golden age of piracy, a range of metals, such as silver, 'iron' (a term that encompassed steel at the time), tin, and pewter, were utilized to craft drug containers[33].

Ceramic drug containers were also widely used in classical antiquity. The earliest jars in the collection are decorated with geometric patterns and deep blue and yellow hues. Historical and religious motifs were commonly utilized for ornamentation during the 17th and 18th centuries. The abbreviations and alchemical symbols found on numerous jars in the collection differed across centuries and countries. Due to variations in spelling and abbreviations for plants, deciphering the labels on drug jars can be challenging, as the same plant could be represented in multiple ways, adding complexity to the interpretation of these labels[34].

Amphorae continued to be used for bulk storage, while smaller vessels like aryballos and lekythoi were employed for more delicate substances. Aryballos were small, round, and often had a single handle, while lekythoi were tall and slender with a slender neck and a solitary handle. Both types of vessels were often used to store oils and perfumes.

the classical period in Greece and Rome saw significant advancements in pharmacy containers, with glassmaking techniques leading to the production of glass bottles and vials for storing liquids and powders. Ceramic drug containers were also widely used, with the earliest jars adorned with intricate geometric designs and vibrant shades of deep blue and yellow. Amphorae continued to be used for bulk storage, while smaller vessels like aryballos and lekythoi were employed for more delicate substances. The use of metal containers, such as lead, silver, and tin, also became more prevalent during this time[35].

Middle Ages

Apothecary:

An archaic term for a medical professional who formulates and dispenses medicine to physicians, surgeons, and patients.

Modern Equivalents:

The roles of apothecaries are now performed by pharmacists and chemists (British English).

Historical Significance:

Investigation of herbal and chemical ingredients by apothecaries was a precursor to modern chemistry and pharmacology.

Range of Services:

Apart from dispensing herbs and medicine, they Provided general medical guidance and services now performed by specialists like surgeons and obstetricians.

Commerce:

Apothecary establishments supplied medicinal compounds and pharmaceuticals in bulk to other healthcare professionals

Control over Tobacco Trade:

In 17th-century England, apothecaries played a significant role in the tobacco trade, as it was initially imported and marketed as a medicinal product.

During the Middle Ages, the use of natural materials for pharmacy containers continued, emphasizing portability and preservation. Apothecaries and herbalists employed fabric pouches crafted from linen or silk to store medicinal herbs, which were practical for carrying and storing due to their compact size and durability also they protected against light and moisture, making them an ideal solution for storing and transporting herbs. Linen, being a breathable and lightweight material, allowed for the proper aeration of the herbs, preventing the growth of mold and mildew. Silk, on the other hand, offered a more luxurious and durable option, providing a protective layer for delicate herbs and roots[12].

During that time, animal skins like parchment and leather played a crucial role in pharmaceutical packaging. These natural materials offered a robust and protective barrier against environmental factors that could potentially degrade the potency of medicines. The durability of animal skins ensured that the packaged medications remained stable and effective, providing a reliable means of storage and transportation for healthcare products. Parchment, made from animal skin, was particularly suitable for storing medicinal documents and herbs due to its strength and resistance to moisture. Leather, with its robust nature, offered a secure and protective casing for medicines, ensuring their preservation during storage and transportation.

throughout the initial decades of the 17th century, pharmacy containers evolved to include tall cylindrical containers made from boxwood or linden wood for the storage of dried botanical drugs. These containers were chosen for their ability to preserve the medicines better than silver, copper, or other metals. The use of these materials reflected the comprehension of the characteristics of various materials and their suitability for storing different types of medicines[36].

Unguents, or ointments, were kept in wooden boxes made of horn or solid woods like ebony, guaiacum, or boxwood. These woods were valued for their ability to protect the unguents from light and moisture, ensuring their potency and effectiveness. The use of these materials demonstrated the resourcefulness and ingenuity of apothecaries and herbalists in utilizing materials that were readily available and effective in preserving medicines.

During Piracy's heyday, various metals were used to craft containers for storing medications. This included silver, metals commonly referred to as "iron" (which often encompassed steel at the time), tin, and pewter. Notably, William Fabry mentions the use of silver in his book on sea and military medicine chests. Silver is mentioned by William Fabry in his book on sea and military medicine chests, while iron or glass vessels were suggested by Jean de Renou for storing turpentine. However, there are no existing mentions of to the use of these metals in sea surgeon's books, suggesting that they may not have been commonly used for this purpose[37].

Tinsmiths Tin laborers were prevalent across Britain by the beginning of the 17th century, and tin was certainly utilized as a material for medicine containers during this period. An example of this usage can be seen in a medicine chest presented to Sir John Clerk of Penicuik by the Grand Duke of Tuscany in 1698, during his visit to Tuscany includes several tin medicine containers, demonstrating the use of this material for pharmacy containers. Tin, being a lightweight and corrosion-resistant metal, offered an ideal solution for storing and transporting medicines[37].

By utilizing materials that were readily available and effective in preserving medicines, these practitioners demonstrated a deep understanding of the importance of proper packaging in maintaining the quality and efficacy of their remedies. The variety of materials used, from fabric pouches and animal skins to wooden containers and metals, demonstrates the understanding of the properties of these materials and their suitability for storing different types of medicines. The evolution of pharmacy containers over time reflects the continuous efforts to overcome challenges and improve the storage and preservation of medicines for the benefit of society.

Renaissance and Early Modern Period

The Renaissance era witnessed a renewed fascination with classical knowledge and scientific inquiry, leading to advancements in pharmacy container design. Glassblowing techniques improved, allowing for the production of a wider range of glass containers with precise shapes and sizes. These glass containers were often adorned with intricate designs and labels, showcasing the sophistication of ancient craftsmanship[14].

Pharmacopoeias and herbal manuals of the Renaissance period included detailed instructions on the proper storage and packaging of medicines. These manuals emphasized the importance of using airtight and light-resistant containers to maintain the potency of medicines. The use of airtight and light-resistant containers became increasingly important during this period, as apothecaries recognized the need to protect medicines from external factors that could compromise their effectiveness For instance, the first pharmacopoeia appeared in Germany in 1546, and The establishment of the Society of Apothecaries in London in 1617 is regarded as the inception of the pharmacy profession[21].

Wooden containers were also used during the Renaissance period for the preservation of dried botanical medicines. Tall cylindrical containers crafted from boxwood or linden wood were employed for this purpose, as they were believed to preserve medicines better than silver, copper, or other metals.

the Renaissance period saw significant advancements in pharmacy container design, with the use of airtight and light-resistant containers becoming increasingly important for maintaining the potency of medicines. Apothecaries used a variety of containers, including glass, metal, and wooden containers, to store and transport medicines. The use of intricate designs and labels on these containers showcased the sophistication of ancient craftsmanship and reflected the importance of pharmacy in Renaissance society[21].

Industrial Revolution and Beyond

The Industrial Revolution marked a transformative period in pharmacy container manufacturing, introducing significant changes that revolutionized the field. Mass production techniques enabled the widespread use of standardized glass bottles, metal tins, and paper packaging for pharmaceutical products. Glass bottles, with their transparency and non-reactive properties, became a popular choice for storing various medicines, ensuring the preservation of their potency and quality.

The standardization of glass bottles during the Industrial Revolution not only improved the efficiency of pharmaceutical packaging but also enhanced safety and hygiene standards. The introduction of labeling regulations and quality control measures played a vital part in ensuring the safety and efficacy of medicines stored in containers. Proper labeling helped pharmacists and consumers identify the contents of the containers accurately, reducing the potential for errors in medication and enhancing patient compliance[3].

Innovations like screw caps, rubber stoppers, and blister packs emerged during the Industrial Revolution, transforming the way medications were packaged and dispensed. Screw caps provided a convenient and secure closure mechanism for glass bottles, ensuring the integrity of the stored medicines. Rubber stoppers offered airtight seals, preventing contamination and maintaining the freshness of liquid medications. Blister packs revolutionized pharmaceutical packaging by offering individualized doses in pre-formed cavities, enhancing convenience, portability, and dosage accuracy[38].

The latest innovations in pharmaceutical packaging

In recent years, there has been a notable influx of innovative technologies and materials within the pharmaceutical packaging sector, aimed at addressing evolving demands and complexities. Here are some of the latest advancements in pharmaceutical packaging:

Smart Packaging: Technological integration into pharmaceutical packaging has led to the development of smart packaging solutions. These packages incorporate sensors, indicators, or electronic components to monitor factors such as temperature, humidity, and light exposure. By providing real-time data on medication storage conditions, smart packaging ensures efficacy and safety, while also improving inventory management and enhancing patient safety through timely alerts about expired or compromised medications[26].

Security-Sealed Packaging: In response to the growing threat of drug counterfeiting and tampering, the implementation of anti-tampering packaging has become increasingly vital. Innovative solutions include seals, labels, or closures that visibly indicate any attempts at tampering with the package. These features uphold the authenticity and safety of pharmaceutical products, thereby safeguarding patients from potential harm and fostering trust in the supply chain.

Environmentally Friendly Packaging: With a heightened focus on environmental sustainability, the pharmaceutical industry is actively exploring eco-conscious packaging alternatives. Biodegradable and recyclable materials, such as plant-based plastics and paper-based packaging, are being embraced to reduce the environmental impact of pharmaceutical packaging. Additionally, companies are optimizing packaging designs to minimize waste and promote sustainable practices across the supply chain[26].

Interactive Pharmaceutical Packaging: Interactive packaging initiatives engage both patients and healthcare professionals by offering additional information and support. Technologies like QR codes, augmented reality (AR), and near-field communication (NFC) are integrated into packaging to provide access to digital content, including dosage instructions, educational materials, and patient support programs. This interactive approach not only enhances medication adherence but also empowers patients with knowledge, enriching the overall healthcare experience[26].

1.3 Evolution Of packaging material for powders

The evolution of packaging materials for powders has been a dynamic journey shaped by technological advancements, changing consumer demands, the need for extended shelf life, and the quest for sustainability in the pharmaceutical industry. Over the years, the packaging landscape for powders has witnessed a remarkable transformation, transitioning from basic protection to sophisticated solutions that ensure product integrity, safety, and convenience. Historically, the primary function of pharmaceutical packaging was to protect medications from physical damage and contamination. Nevertheless, as drug formulations have become increasingly complex, there has been a shift away from traditional materials such as glass containers and aluminum foils, towards a diverse range of options including plastics, polymers, and specialized coatings[4].

Smart packaging solutions have emerged as a prominent trend in the pharmaceutical sector, integrating sensors, RFID tags, and NFC chips to enable real-time monitoring of product integrity and usage. These cutting-edge technologies not only enhance safety and compliance but also facilitate personalized patient engagement through features like dosage reminders and medication tracking. By incorporating smart packaging solutions, the pharmaceutical industry is embracing a new era of packaging innovation that prioritizes efficiency, patient-centric care, and the seamless integration of technology to meet the evolving needs of both consumers and regulatory standards[4].

Early Packaging (Pre-Industrial Era)

In the Pre-Industrial Era, the packaging of powders was a crucial aspect of daily life, trade, and cultural practices. The early packaging methods were characterized by their simplicity, functionality, and reliance on natural resources. Clay containers were among the most prevalent forms of packaging for powders, with their abundance and malleability making them an ideal choice for storing and transporting various substances. Clay pots and vessels were handcrafted by skilled artisans, who molded and fired the clay to create durable and airtight containers that could protect powders from moisture, contaminants, and external elements.

Stone containers, while less common than clay vessels, were highly valued for their durability and resilience. Stone, being a sturdy and long-lasting material, provided enhanced protection for powders, safeguarding them from external elements and maintaining their quality over extended periods. Stone containers were frequently adorned with intricate carvings and decorations., showcasing the skill and craftsmanship of ancient artisans. These containers were not only functional but also symbolic of the cultural values and artistic expression of the societies that used them.

Bone containers, crafted from animal bones, represented another innovative approach to packaging powders in the Pre-Industrial Era. Bones were utilized for their strength and versatility, providing a unique material for creating small, intricate containers for powders. Bone containers were often intricately carved with intricate designs or symbols, serving not only as functional storage vessels but also as decorative artifacts. The use of bone containers for powders demonstrated the resourcefulness and ingenuity of ancient civilizations in utilizing natural materials to meet their packaging needs.

he early packaging methods for powders in the Pre-Industrial Era were essential for preserving the potency and quality of medicinal powders, spices, and other powdered substances. These primitive containers laid the foundation for the evolution of packaging materials, setting the stage for the advancements that would follow in subsequent eras. The simplicity and functionality of these early packaging materials highlight the ingenuity of ancient civilizations in developing solutions to meet their storage and transportation needs[26].

The use of natural materials for packaging powders in the Pre-Industrial Era was a reflection of the limited technological advancements of the time. However, these early packaging methods were effective in preserving the integrity and potency of the powders they contained. The use of clay, stone, and bone containers for powders showcased the resourcefulness and adaptability of ancient civilizations in utilizing the materials available to them to meet their packaging needs.

The development of early packaging methods for powders was also influenced by cultural practices and beliefs. For instance, certain powders were considered sacred or had symbolic significance in religious rituals. The packaging of these powders was often intricate and decorative, reflecting their cultural importance. The use of decorative motifs, symbols, and colors in early packaging materials was a way to communicate the significance of the powders they contained, highlighting the importance of packaging in preserving and presenting valuable commodities.

The evolution of packaging materials for powders in the Pre-Industrial Era was a gradual process, characterized by incremental improvements and adaptations to the materials and techniques used. The development of new packaging methods was driven by the need to preserve and protect powders, as well as by the desire to create more efficient and convenient storage solutions. The early packaging methods laid the groundwork for the advancements in packaging technology that would shape the future of the industry.

The technology used for powders packaging in the Pre-Industrial Era was primarily based on natural materials such as leaves, gourds, animal skins, and wooden crates. These materials were used for storing, protecting, and transporting goods, including food and other commodities. As civilizations progressed, more durable materials like pottery, clay, and metal containers were developed. For instance, glass packaging was first used in Egypt around 1500 B.C., with glass pots being mixed with melted limestone, soda, sand, and silicate to create glass packaging

In the Middle Ages, Europeans began using wooden barrels for storing food. These barrels were filled with various types of food, such as vegetables, fruits, grains, and meat products, as well as wine, oil, and other goods. In the 16th century, paper packaging gained popularity among Europeans, who utilized it for transporting various goods, including food, during colonization endeavors due to its lightweight and easy transportability. During the 18th century, the evolution of paper packaging extended to the creation of packages specifically designed for storing tobacco. These packages, constructed from paper with wireframes, facilitated convenient storage and smoking of tobacco. The discovery of carton material was serendipitous, attributed to Robert Gair's observation that cutting and creasing paperboard simultaneously offered enhanced benefits. This led to the invention of the first automated carton, now recognized as "semi-flexible packaging."

The first commercial cardboard box was introduced in England in 1817, with the Chinese inventing this material more than 200 years before the commercial box was produced. The first commercially successful shipping cartons were invented by Sir William Parry in 1852, typically made of wood and capable of holding up to 20 tons of cargo. It was not until 1925 that the first steel shipping container was developed properly and professionally by George Steers Jr., revolutionizing shipping by reducing the amount of cargo that needed to be transported on ships[10].

Industrial Era

The Industrial Revolution was a significant period for the evolution of packaging materials, particularly for powders. During this era, glass jars and bottles were introduced, which offered several advantages for powder packaging. Glass containers provided transparency, Consumers were provided with visibility of the product., which was a significant advantage for marketing purposes. Additionally, glass containers offered improved barrier properties, protecting the powders from moisture, light, and contaminants, ensuring the product's quality and safety.

However, glass containers also had limitations. They were heavy, making them less practical for transportation and handling, and prone to breakage, which could lead to product loss and safety concerns. Despite these limitations, glass containers remained a popular packaging material for powders due to their transparency and barrier properties[26].

During the latter part of the 19th century and the initial decades of the 20th century,, paper and cardboard boxes specifically designed for powders were developed. These boxes featured inner liners and improved sealing techniques, providing better protection for the powders during transportation and storage. Additionally, the introduction of folding cartons allowed for efficient storage and transportation, reducing the risk of damage and product loss.

These advancements in paper and cardboard packaging materials provided a lightweight and cost-effective alternative to glass containers. However, they also had limitations, such as reduced barrier properties compared to glass, which could affect the product's quality and safety. Despite these limitations, paper and cardboard packaging materials remained a popular choice for powder packaging due to their affordability and convenience[32]

The evolution of packaging materials for powders in the industrial era has been marked by significant advancements in technology and design. In the early stages of the industrial era, glass jars and paperboard boxes became popular for packaging powders, providing durability and protection for goods during transportation. However, the invention of plastic and the cardboard box revolutionized the packaging industry, offering versatility, durability, and ease of use.

During the industrial era, the development of modern powder packaging technologies was crucial for the manufacturing industry. Tools and drives, such as auger powder filling machines, were used to accurately fill and package powders**.** These machines were designed to handle various product characteristics, such as accuracy level, dosing rate, fill weight, and neck of containers.

Gravimetric powder filling technology was also introduced during this era, allowing for precise fill-by-weight filling. This technology helped address common issues associated with non-fill-by-weight types of equipment, such as variable product density, inconsistent tare weight, compromising crucial fill weight, and occasional variation of proper fill weight[1].

Volumetric filling technology was another significant advancement in powder packaging during the industrial era. This technology is based on the fill capacity, with the number of revolutions of an auger directly proportional to the quantity filled in the container. This principle is suitable for either one or multiple augers, whether using semi or completely automatic machines.

In addition to these technological advancements, the industrial era saw the introduction of new materials for packaging powders. Plastic, in particular, became a popular choice due to its versatility and durability. Zipper-seal bags, for example, were invented in 1954 and quickly became popular for food storage, including Ziploc bags for individual use[8].

The Rise of Plastics

The mid-20th century marked the introduction of plastics, which had a revolutionary impact on powder packaging. Plastic materials, such as polyethylene and polypropylene, became popular for packaging powders due to their flexibility, resistance to moisture and chemicals, and lightweight nature. Plastic bags, pouches, and containers became commonplace in the packaging of powdered goods, such as food, pharmaceuticals, and chemicals[8].

The development of flexible plastic pouches and bags offered lightweight, cost-effective, and versatile options for various powder products. These plastic pouches and bags provided better protection and preservation of powdered goods during transportation, reducing the risk of damage and spoilage. Additionally, plastic pouches and bags were more convenient for consumers, as they were easy to open, close, and store.

However, the rise of plastics has also brought about growing environmental concerns surrounding plastic waste. Plastic waste in the environment is unacceptable, and the plastics industry is working towards reducing greenhouse gas emissions and tackling climate change through the use of alternative feedstocks and renewable energy.

the introduction of plastics in the mid-20th century had a revolutionary impact on powder packaging, offering lightweight, cost-effective, and versatile options for various powder products. However, the growing environmental concerns surrounding plastic waste require the development of more sustainable alternatives, such as biodegradable and compostable plastics[8].

Modern Innovations

The evolution of packaging materials has been a significant factor in preserving the quality and preventing caking of hygroscopic powders. moisture-control technologies has been a significant innovation in the packaging industry. These technologies include the use of desiccant packets, which are small packets containing materials that absorb moisture, preventing it from reaching the powdered product. This is particularly important for hygroscopic powders, which are prone to absorbing moisture from the environment, leading to caking and reduced quality. Desiccant packets are often included in packaging for pharmaceuticals, food ingredients, and other sensitive products[8].

Another moisture-control mechanism is the use of resealable closures, which allow the packaging to be closed tightly after each use, reducing the exposure of the powdered product to moisture and other external factors. This is particularly important for products that are used frequently or in humid environments, as it helps to maintain the quality and safety of the product over time.

Single-serve and pre-measured powder packaging has also become increasingly popular in recent years. This type of packaging is designed to provide convenience and portion control for consumers, making it an ideal solution for on-the-go consumption. Blister packs and stick packs are two common types of packaging used for single-serve and pre-measured powders. Blister packs are typically made from a combination of plastic and aluminum, providing a barrier to moisture, light, and oxygen. Stick packs, on the other hand, are made from a single layer of film, which is designed to be flexible and easy to tear.

The use of biodegradable and compostable plastics has become increasingly popular in recent years, as concerns over plastic waste and its impact on the environment have grown. These materials offer a more sustainable alternative to traditional plastics, as they can be broken down by microorganisms in the environment, reducing the amount of waste that ends up in landfills and oceans. However, there are still challenges to be addressed in terms of the cost and performance of these materials, as they may not be as durable or as effective as traditional plastics in certain application.

The use of smart packaging technologies is another emerging trend in the packaging industry. These technologies include the use of sensors, RFID tags, and NFC chips to provide real-time monitoring of product integrity and usage. This can help to enhance safety and compliance, while also enabling personalized patient engagement through features such as dosage reminders and medication tracking.

child-resistant packaging, and a focus on sustainability and safety are all key factors shaping the future of pharmaceutical packaging.

Conclusion to chapter 1

1-Medicinal powders have evolved from ancient soaking methods to finely ground formulations, offering customization for patient needs. Despite challenges, powders remain vital for drug administration. While tablets and capsules are popular, powders, including advancements like metal powders, continue to play a significant role in pharmaceutical science, reflecting a legacy of innovation in alleviating human afflictions.

2-The evolution of pharmacy containers is a fascinating journey reflecting advancements in materials, technology, and our understanding of medication needs. From basic clay pots in ancient civilizations to smart packaging today, the focus has remained constant: protecting and preserving medications. Early containers like animal bladders and glass bottles offered basic protection, while the Middle Ages saw fabric pouches and wooden containers prioritize portability. The Renaissance ushered in airtight and light-resistant containers, recognizing the importance of proper storage for potency. The Industrial Revolution brought mass production of standardized glass and metal containers, boosting safety and efficiency. Today, innovations like smart packaging, security seals, and eco-friendly materials address new challenges and patient needs. This continuous evolution, merging historical knowledge with cutting-edge technologies, underscores the critical role of containers in maintaining medication integrity and efficacy throughout history and into the future.

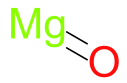
CHAPTER 2

OBJECTS AND METHODS OF RESEARCH

2.1 Objects of research

In the study of the pharmaceutical market of medicinal products in sachet packaging, the existing assortment listed in the State Register of Medicinal Productsof Ukraine was used as an object .

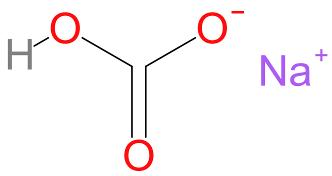
Magnesium oxide (SFU 2nd edition, supplement 2, p. 421)



Magnesium oxide is an oxide with the formula MgO. It consists of Mg^{2+} andO^{2-} ions, between which ionic bonds are formed. Magnesium oxide has a crystallinestructure similar to sodium chloride. It is a light, loose white powder, extremely hygroscopic.

Magnesium oxide occurs naturally in the minerals periclase, magnesite, brusite, and spinel.

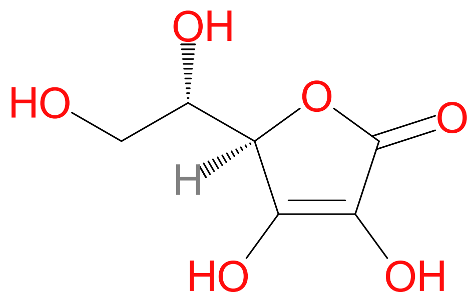
Sodium bicarbonate (SPU 2nd edition, supplement 2, p. 475)



Sodium bicarbonate or sodium bicarbonate is a chemical compound with theformula $NaHCO_3$, a white solid with a slight salty-alkaline taste that resembles that of washing soda (sodium carbonate). Its natural form is the mineral nachcolite. Thecommon name "sodium bicarbonate" is due to the name of the bicarbonate ion (HCO_3), which is widely involved in biochemical processes in the body. It is one

of the mineral components of natural water sources. It is found in dissolved form inbile, where it serves to neutralize the acidity of hydrochloric acid, which is producedin the stomach and excreted into the duodenum of the small intestine. This substance has been known since ancient times and was widely used in soap making. It is commonly called baking soda. The Latin (medical) name is Natrium carbonicum monobasicum, or Natrii hydrocarbonas[5].

Ascorbic acid (GMP 2nd edition, supplement 2, p. 61)

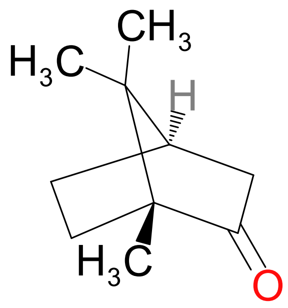


Ascorbic acid (gamma-lactone of 2,3-dihydro-L-gulonic acid, vitamin C) $C_6H_8O_6$, a relatively simple organic acid found in fresh fruits (apples, plums, peaches,etc.) and vegetables.

It is not synthesized in the human body and is supplied only with food. It dissolves in water and is destroyed by prolonged boiling, so soaking or processing vegetables reduces their vitamin C content. A large amount of vitamin C is found inlemons (38-60 mg/100 g), rose hips (650 mg/100 g), bell peppers (250 mg/100 g), currants (200 mg/100 g), and green onions. The daily human need for ascorbic acidis quite high - 63-105 mg. Lack of ascorbic acid can lead to scurvy. It was discovered in 1934 by Thaddeus Reichstein, a Swiss chemist and Nobel Prize winner[20].

Vitamin C performs two main tasks in the body: providing immune protectionand stabilizing mental activity. Vitamin C is the best way to preserve vitality. Whenpeople lack C, they experience bleeding gums, frequent colds, the risk of inflammation of the mucous membranes, excess weight, fatigue, weak nerves, poorconcentration, depression, insomnia, early wrinkles, and problems with the cardiovascular system[20].

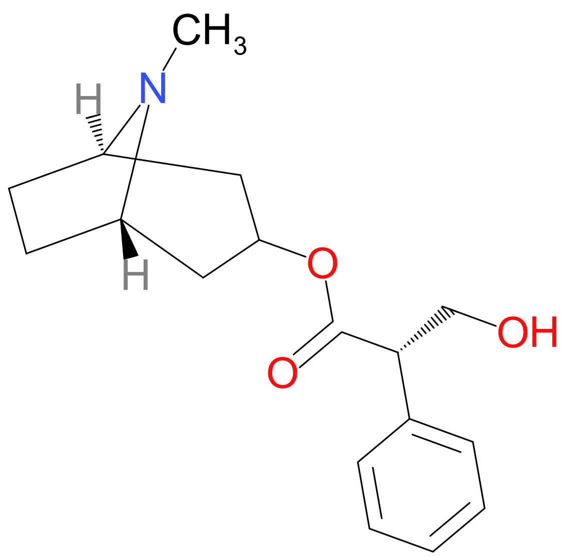
Camphor (SPU 2nd ed., Supplement 2, p. 343)



Camphor is a waxy, flammable, white or transparent solid with a strong aromatic odor. It is a terpenoid with the chemical formula $C_{10}H_{16}O$.It is found in the wood of the camphor laurel (Cinnamomum camphora), a large evergreen tree that grows in Asia (particularly in Sumatra, Borneo and Taiwan), and the Borneo camphor tree (Dryobalanops Aromatica), a giant of the forests of Borneo. It also occurs in some other related trees of the laurel family, especially Ocotea usambarensis. The dried leaves of rosemary (Rosmarinus officinalis) from the family of the Thistle family contain up to 20% camphor. It can also be syntheticallyproduced from turpentine. It is valued for its odor, and is used as an ingredient in cooking (mainly in India), as an embalming liquid, for medicinal purposes, and in religious ceremonies. The main source of camphor in Asia is camphor basil[15].

Extract of holly (SPU 2nd edition, supplement 3, p. 244)

hyoscyamine



The extract is dry, standardized, obtained from the raw material described in the monograph "Belladonna leaves". Content: from 0.95% to 1.05% of the total alkaloids, in terms of hyoscyamine ($C_{17}H_{23}NO_3$; M.M. 289.4) and dry extract.

All substances used met the requirements of the relevant regulatory.

2.2Research methods

<u>Appearance</u>

The appearance of API powders was studied in accordance with the "Description" section of the relevant articles on the substance (see Section 2.1).

<u>Average weight</u>

The average weight of the studied powders was determined in accordance with SPS, ed. 2, Vol. 1, p. 2.9.5. The series was considered to be consistent in this respect if no more than two of the 20 samples had a deviation from the average weight of more than ± 5 %, and none of the individual masses deviated from the average by more than ± 10 %.

<u>Weight loss during drying</u>

It was carried out according to the SPS method 2, supplement 2, 2.2.32. Drying to a constant mass means that the results of 2 consecutive weighing do not differ by more than 0.5 mg, the second weighing is carried out after an additional drying period of at least 30 minutes under the conditions specified for the test substance.

<u>Identification</u>

The identification of APIs in the studied powders was carried out by the following methods:

- magnesium oxide: 2.3.1 Qualitative reaction to magnesium ions;
- sodium bicarbonate: 2.3.1 Qualitative reaction to sodium ions;
- camphor: 2.2.7 Optical rotation;
- ascorbic acid: Qualitative reaction (SFC 2nd edition, supplement 2, p.61);
- extract of beautyberry: 2.2.27 TLC.<u>Quantification</u>

Quantitative determination of APIs in the studied powders was performed by the following methods:

- magnesium oxide: 2.5.11 Complexometry;
- sodium bicarbonate: Titration;

- camphor: 2.2.28 TSC Impurities;
- ascorbic acid: Titration;
- extract of beautyberry: 2.2.27 TLC.

The statistical analysis of the study results was conducted in accordance with the requirements of SPU 2.1, section 5.3 using statistical and mathematical analysis methods.

Conclusions to Chapter 2

1. The properties of the research objects, in particular, the active pharmaceutical ingredients (magnesium oxide, sodium bicarbonate, camphor, ascorbic acid, belladonna extract) used in the experimental part are described.
2. The methods and conditions of economic, physicochemical, pharmaco-technological tests used to study the effect of packaging material on the stability of powders during storage are selected and described.

CHAPTER 3

STUDY OF THE STABILITY OF PHARMACY POWDERS IN SACHETS OF DIFFERENT TYPES

3.1 Analysis of the United State of America Market for Powders in Sachets

North American Pharmaceutical Sachet Market Poised for Growth

The North American market for sachet packaging in pharmaceuticals is brimming with potential, with revenue expected to surpass US$612.1 million by 2027. This translates to a steady growth rate of 5.3% over the forecast period (2020-2027).

Fueling the Rise of Sachets:

A key driver of this growth is the surging demand for over-the-counter (OTC) medications. These readily available remedies for common ailments like colds, allergies, and pain relief offer a convenient and cost-effective solution for consumers. Their widespread availability across drugstores, grocery stores, and mass merchandisers further cements their popularity. A 2019 report by the U.S. Consumer Healthcare Products Association (CHPA) highlights the significant impact of OTC drugs, estimating they contribute a staggering US$146 billion annually to the American healthcare system[9].

Sachet Advantages: A Winning Combination:

The inherent benefits of sachet packaging play a significant role in propelling market growth. Compared to traditional packaging, sachets require less material, leading to reduced storage space needs and lower shipping costs. This translates to overall cost savings for manufacturers. Additionally, the high degree of customization offered by sachets allows pharmaceutical companies to tailor the size, shape, and design of the packaging to perfectly suit their brand and product. This flexibility also creates a prime canvas for effective branding, with the large surface area of sachets providing ample space for logos, product information, and marketing messages[9].

Market Landscape:

The United States currently holds the dominant position within the North American market, capturing a commanding 85% share of revenue in 2019. Canada follows closely behind. This dominance can be attributed to factors like the larger population base in the US and a well-established OTC market.

Looking Ahead:

With the increasing demand for convenient and cost-effective healthcare solutions, the North American market for sachet packaging in pharmaceuticals is poised for continued growth. Manufacturers who capitalize on the advantages of sachets and cater to the evolving needs of consumers are well-positioned to capitalize on this promising market trend.

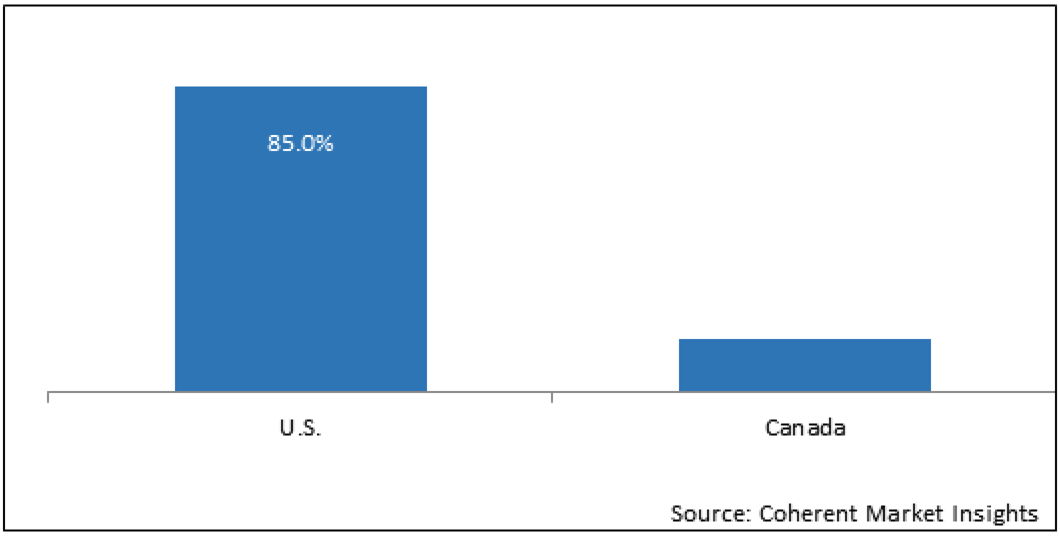


Figure 3.1. North America Sachet Packaging in Pharmaceuticals Market Revenue Share (%), By Country, 2019

The North American Sachet Market: A Growth Story with Challenges

While the North American market for sachet packaging in pharmaceuticals presents a promising future, there are challenges that could hinder its growth. One such challenge is the presence of compelling substitutes within the realm of flexible packaging.

The Rise of Alternative Packaging Solutions:

The availability of other flexible packaging options like stick packs and pouches poses a significant threat to the dominance of sachets in the pharmaceutical market. These alternative solutions offer distinct advantages that could sway manufacturers and consumers alike[9].

Cost Considerations: Sticking to Savings:

Stick packaging, for example, presents a strong economic argument. Due to its design, it often requires less raw material compared to sachets. This translates to lower overall packaging costs for manufacturers. In a competitive market where cost efficiency is paramount, this economic advantage can be a major deciding factor for companies choosing packaging solutions for their pharmaceuticals[9].

Beyond Cost: Exploring Additional Benefits of Substitutes:

The appeal of alternative packaging goes beyond just cost. Pouch packaging, for instance, might offer increased functionality or improved product visibility compared to traditional sachets. This additional functionality could be particularly attractive for certain pharmaceutical products.

Navigating the Competitive Landscape:

Sachet manufacturers in North America must be aware of these evolving trends and the potential of substitute packaging solutions. By focusing on innovation and highlighting the unique benefits of sachets, such as their portability, ease of use, or suitability for single-dose applications, manufacturers can carve out a strong position in the market. Additionally, exploring new materials or functionalities for sachets could help them remain competitive in the face of evolving options[9].

In conclusion, while the North American sachet packaging market for pharmaceuticals exhibits promising growth potential, the presence of readily available substitutes like stick and pouch packaging presents a challenge. By emphasizing the unique advantages of sachets and exploring innovative solutions, manufacturers can ensure their continued success in this dynamic market.

North America Sachet Packaging in Pharmaceuticals Market Report Coverage

<table>
<tr><th>Report Coverage</th><th colspan="3">Details</th></tr>
<tr><td>Base Year:</td><td>2019</td><td>Market Size in 2019:</td><td>US$ 406.1 Mn</td></tr>
<tr><td>Historical Data for:</td><td>2017 and 2018</td><td>Forecast Period:</td><td>2020 to 2027</td></tr>
<tr><td>Forecast Period 2020 to 2027 CAGR:</td><td>5.3%</td><td>2027 Value Projection:</td><td>US$ 612.1 Mn</td></tr>
<tr><td>Geographies covered:</td><td colspan="3">▪ North America: U.S. and Canada</td></tr>
<tr><td>Segments covered:</td><td colspan="3">▪ By Material Type: Plastic (Polyethylene (PE), Polypropylene (PP), Polyethylene Terephthalate (PET), Ethylene Vinyl Alcohol (EVOH), and Others), Aluminum Foils, Paper, and Others
▪ By Packaging Sizes: 01ml-10ml, 11ml-20ml, 21ml-30ml, and Others
▪ By Application: OTC Drugs, Health Beauty Products, and Others</td></tr>
<tr><td>Companies covered:</td><td colspan="3">Ahlstrom-Munksjo, Amcor plc, American Flexpack, Constantia Flexibles, Glenroy Inc., Multi-Pack Solutions LLC, Ropack, Inc., Sharp, Synchpack, and Tripak Pharmaceuticals</td></tr>
<tr><td>Growth Drivers:</td><td colspan="3">▪ Growing demand for OTC drugs
▪ Advantages associated with sachet packaging</td></tr>
<tr><td>Restraints & Challenges:</td><td colspan="3">▪ Availability of substitutes</td></tr>
</table>

Market Constraints

The North American sachet packaging market faces a significant challenge due to the availability of alternative flexible packaging options like stick packaging and pouch packaging. These alternatives offer cost advantages, such as lower raw material expenses and overall packaging costs, which are expected to hinder the growth of sachet packaging in the pharmaceutical sector.

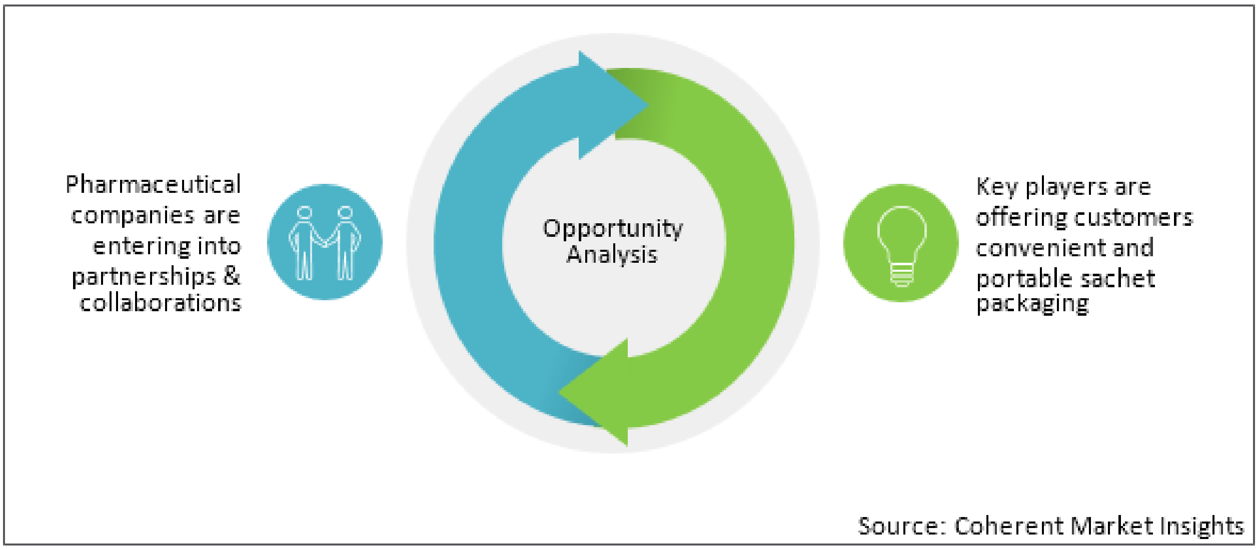


Figure 3.2. North America Sachet Packaging in Pharmaceuticals Market – Opportunity Analysis

In 2019, the plastic segment held a significant revenue share of 40.8% based on material type. This plastic segment is subdivided into polyethylene (PE), polypropylene (PP), polyethylene terephthalate (PET), ethylene vinyl alcohol (EVOH), and other materials. PE is extensively employed in pharmaceutical sachet packaging, particularly for drugs that require refrigeration. It is commonly utilized in pharmaceutical products that are sensitive to oxygen exposure, as it can impact the quality of the packaged pharmaceutical sachets and diminish their shelf life[9].

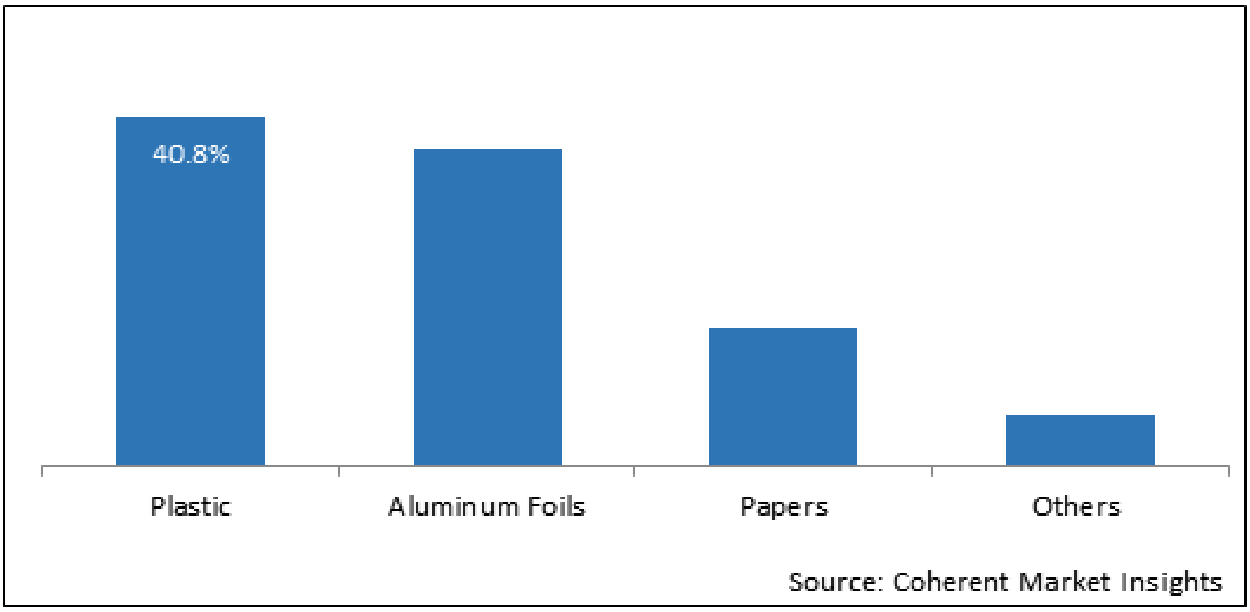


Figure 3.3. North America Sachet Packaging in Pharmaceuticals Market

Revenue Share (%), By Material Type, 2019

North America Sachet Packaging post COVID-19

The SARS COV-19 pandemic has significantly altered consumer purchasing habits, with nationwide lockdowns leading to a spike in panic buying of essential food and hygiene products. This surge in demand has had a substantial impact on the packaging industry as well. Following the latest pandemic, an increasing number of individuals are choosing self-medication over seeking medical advice, resulting in a rise in the stockpiling of over-the-counter drugs like paracetamol and ibuprofen for symptom relief. Moreover, heightened consumer awareness of preventive health measures has driven the demand for immunity-boosting products and health supplements. This overall increase in pharmaceutical demand is expected to propel the growth of the North American sachet packaging market in the pharmaceutical sector during the pandemic[9]..

Industry Rivalry

The North American market for sachet packaging in pharmaceuticals is served by several prominent players, including Amcor plc, American Flexpack, Constantia Flexibles, Ahlstrom-Munksjo, Glenroy Inc., TripPak Pharmaceuticals, Multi-Pack Solutions LLC, Ropack Inc., Sharpand, Synchpack,

3.2 Study of the influence of sachet packaging material on the shelf life ofpharmacy powders

In pharmacy practice, powders can be packed in sachets in two ways: automated (automatic filling line) or manual (manual filling of the sachet with its subsequent sealing).

The automated packaging line (Fig. 3.4) includes the following operations: feeding the packaging material, forming the sachet, sealing the bottom edge, fillingthe sachet with a dose of powder, sealing the top edge, and applying labeling.

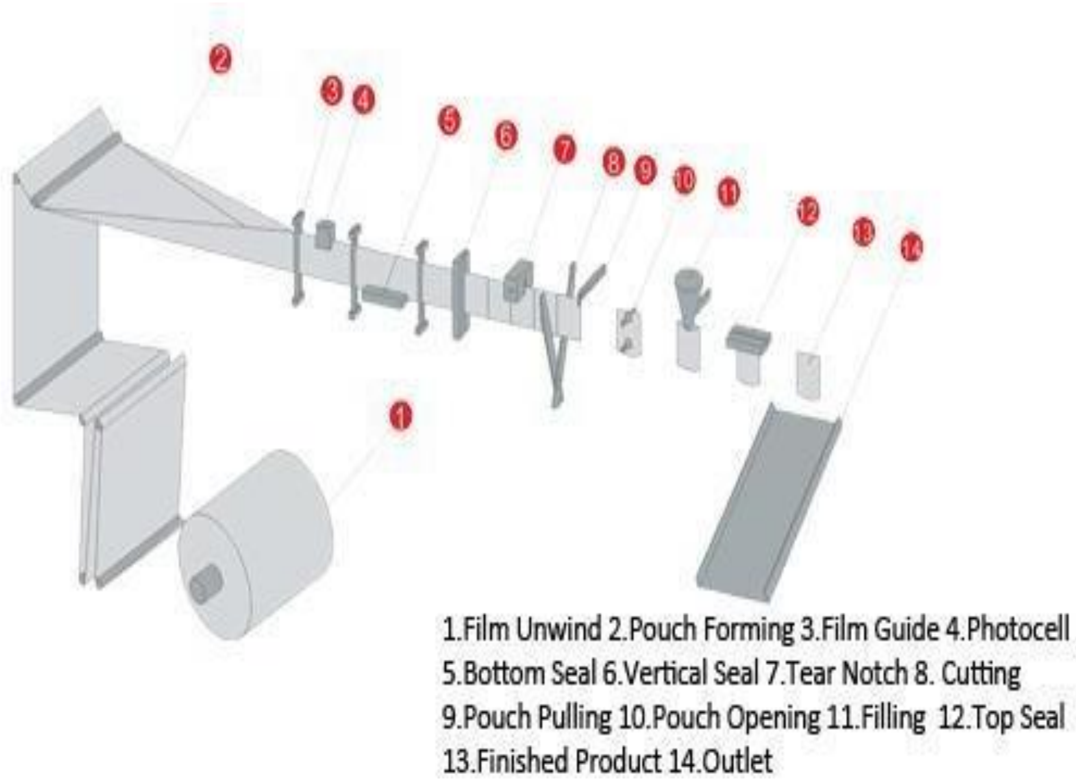


Fig. 3.4 Automated line for packing powders in sachets

Fig. 3.5 Manual sachet filling welder

Manual filling of sachets (Fig. 3.5) involves the use of ready-made sachets, into which the pharmacist manually adds a weighed amount of powder and seals thetop edge of the sachet.

In our study, we used the method of manual filling and sealing of sachets using the FS-200/5 handheld welder.

Based on the research of the range of materials for medical and pharmaceutical sachets, the following materials were selected: Foilbond, Transobond, Transofoil, Transoflow.

Foilbond® has a thin inner layer of aluminum foil that provides excellent protection against moisture, light and oxygen, while the outer paper layer provides ease of opening and consumer convenience.

Transobond is a multilayer laminate film suitable for use on high-speed horizontal (HFFS) and vertical (VFFS) folding and sealing machines with longitudinal corner folding and sealing. Alternatives with high-performance sealing layers of low or high barrier protection class guarantee optimum performance.

Transofoil® has a thin inner layer of aluminum foil that provides excellent protection against moisture, light and oxygen, while the outer layer provides strength and the ability to apply stunning visual effects. The superior polyethylene and ionomer-based seal, excellent resistance to hot adhesion and stress cracking make itsuitable for use in the harshest barrier protection environments and provide high processing performance.

Available with a silver or white outer surface, it provides a great, eye-catching background for high-quality printing.

Transoflow is a versatile multilayer film for bags or flow packs for product individualization.

The range of sealing layers from economical thin OPP to high performance polyethylene grades enables efficient packaging for a wide variety of products in high-speed packaging machines.

For UV protection and a great appearance, the good moisture barrier can be supplemented with a metallized option. Additional laser perforation allows for easyopening of the packaging or extending the shelf life of breathable products.

Based on the research, 4 types of packaging material were selected for the production of sachets: Foilbond, Transobond, Transofoil, Transoflow. Samples of API powders with different physical and chemical properties were placed in sachets made of the selected material and stored for 6 months.

Representatives of different groups were selected to cover different physical and chemical properties:

- Magnesium oxide is lightweight;
- sodium bicarbonate;
- camphor;
- ascorbic acid;
- extract of hollyhock.

SODIUM BICARBONATE

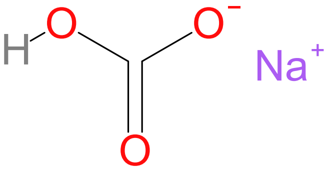


Fig. 3.6 Sodium bicarbonate

(PFC), Natrii hydrogenocarbonas(PhEur), Sodium bicarbonate (BP, JP USP), Carbonic acid monosodium salt (CAS No. 144-55-8); syn: Baking soda; E500; Effer- Soda; sodium acid carbonate; sodium hydrogen carbonate is a white, transparent, odorless powder with a salty alkaline taste, containing NaHCO3 in the range of 99.0- 101.0%. The crystal structure is monoclinic prisms. Varieties with different particle sizes are commercially available, from well-flowing powder to well-flowing homogeneous granules.

MAGNESIUM OXIDE

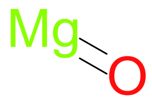


Fig. 3.7 Magnesium oxide

(SFS), Magnesii oxidum ponderosum (Magnesium oxide, heavy) and Magnesii oxidum leve (Magnesium oxide, light) (PhEur), Magnesium oxide (JP, USP, CAS No. 1309-48-4), Heavy magnesium oxide and Light magnesium oxide (BP); syn: Calcined magnesia, calcined magnesite, Destab, E530, Magcal, Magchem 100, Maglite, magnesia, magnesia monoxide, magnesia usta, magnyox is a fine, odorless, white powder whose crystals have a cubic crystal lattice (α=0.4213 nm, z=4, space group Fm3m). The mineral is naturally occurring periclase [7]

CAMPHORA RACEMIC

Fig. 3.8 Camphor

(Camphora racemica), (1RS,4RS)-1,7,7- trimethylbicyclo[2.2.1]heptan-2-one. API of semi-synthetic origin. White crystalline powder or brittle crystalline mass, very volatile at room temperature, slightly soluble in water, readily soluble in alcohol, ether and petroleum ether, readily soluble in fatty oils, very slightly soluble in glycerin. Melting point - 172-180 oC. [α]20D = +0.15o to -0.15o (10% solution in alcohol). UV spectrum: λmax = 289 nm (784658 = 2.07) in methanol. Store in a tightly sealed container [15].

ASCORBIC ACID

Fig. 3.9 Ascorbic acid

Acidum ascorbicum (PhEur); Ascorbic acid (BP, JP, USP); L-(+)-Ascorbic acid (CAS No. 50-81- 7); syn: C-97; cevitamic acid; 2,3-didehydro- L-threo-hexono-1,4-lactone; E300; 3-oxo-L- gulofuranolactone, enol form; vitamin C is a white or yellowish, odorless, non-hygroscopic crystalline powder or colorless crystals with a pronounced sour taste [20].

BELLADONNA EXTRACT

Fig. 3.10 Extract of the hollyhock

Standardized dry extract of belladonna leaves is obtained from belladonna leaves (0221). It contains not less than 0.95% and not more than 1.05% of total alkaloids, calculated on hyoscyamine ($C\ H_{1723}\ NO_3$, Mr 289.4) relative to the dried extract [11].

The studied samples are presented in Table 3.3

Table 3.3

Tested samples of powders in sachets, placed in storage (n=5)

Composition and type of packaging material		Sample
Magnesium oxide light	Foilbond	1a
	Transobond	1b
	Transofoil	1c
	Transoflow	1d
Sodium bicarbonate	Foilbond	2a
	Transobond	2b
	Transofoil	2c
	Transoflow	2d
Camphor	Foilbond	3a
	Transobond	3b
	Transofoil	3c
	Transoflow	3d
Ascorbic acid	Foilbond	4a
	Transobond	4b
	Transofoil	4c
	Transoflow	4d
Extract of thehollyhock	Foilbond	5a
	Transobond	5b
	Transofoil	5c
	Transoflow	5d

Each sample was represented by a series of 5 samples. The powder quality was tested every month. The initial quality indicators of the relevant regulatory documents were used as a standard for comparison.

Before being stored, the APIs were thoroughly ground in a mortar and pestle to obtain a homogeneous fine powder. Grinding was performed in accordance with the general rules of pharmacy drug technology. The quality of grinding was controlled by sieve analysis. The quality of the samples was assessed by such quality indicators as appearance, average weight, percentage of moisture, identification andquantification.

The data of the initial analysis at the beginning of the experiment and the requirements of the SPU are presented in Table 3.4.

The quality of each sample was analyzed on a monthly basis according to thespecified parameters. The results are shown in Table 3.5.

According to the "Appearance" indicator, during the first 4 months of storage, all samples showed a result that meets the requirements of the SPU. At 5 and 6 months of storage, samples 3b, 3d, 4b, 4d, 5b, 5d had inadequate results. In particular, samples of camphor (3b, 3d) after 5 months of storage contained lumps of powder and a certain amount of liquid, which indicates its melting. Samples of ascorbic acid (4c, 4d) after 5 months of storage had changes in color - slight yellowing, indicating an insufficient level of protection from light. The samples of the extract of the rosemary (5b, 5d) contained lumps of powder after 5 months of storage.

Table 3.4

SPU requirements and initial analysis of the selected AFIs

Indicat	**AFI**	**Requirements of the State Pharmacopoeia of Ukraine**	**Data from the initial analysis**
1	**2**	**3**	**4**
Appearance	Magnesium oxide light	Description. SPU 2nd edition, supplement 2, pg. 421	Fine, white, amorphous powder
	Sodium bicarbonate	Description. SPU 2nd edition, supplement 2, pg. 475	White crystalline powder

1	2	3	4
	Camphor	Description. SPU 2nd edition, supplement 2, pg. 343	White crystalline powder or crumbly crystallinemasses, very volatile even at room temperature
Average weight	Ascorbic acid	Description. SPU 2nd edition, supplement 2, pg. 61	White or almost white crystalline powder or colorless crystals that are discolored by air and moisture
	Extract of the hollyhock	Description. EP, 01/2005:1294	Hygroscopic powder of brown or greenish color
	Magnesium oxide light	SPU, 2.1, 2.9.5 Deviation from the average weight is more than ± 5 %	5,0 ± 0,21 d
	Sodium bicarbonate		5,0 ± 0,22 d
	Camphor		5,0 ± 0,19 d
	Ascorbic acid		5,0 ± 0,19 d
	Extract of the hollyhock		5,0 ± 0,21 d
Weight loss during drying	Magnesium oxide light	SPU 2.2, 2.2.32 Drying to constant weight means that the results of 2 consecutive weighings do not differ by more than 0.5 mg, the second weighing is carried out after an additional drying period of at least 30 minutes under the conditions specified for the test substance.	0,05 d
	Sodium bicarbonate		0,09 d
	Camphor		---
	Ascorbic acid		0,05 d
	Extract of the hollyhock		0,17 d

1	2	3	4
Identification	Magnesium oxide light	2.3.1 Qualitative reaction to magnesium ions	Dissolve 15 mg of powder in 2 ml of dilute nitric acid P and neutralize with dilute sodium hydroxide solution R. The resulting solution reacts with magnesium ions.
	Sodium bicarbonate	2.3.1 Qualitative reaction to sodium ions	Dissolve 5.0 g of powder in 90 mL, add water P without carbon dioxide, and bring to 100.0 mL. The resultingsolution reacts with sodium ions.
	Camphor	2.2.7 Optical rotation	+0.15° to -0.15°
	Ascorbic acid	Qualitative response	To 1 ml of powder solution add 0.2 ml of dilute nitric acid and 0.2 ml of silver nitrate solution. A grayprecipitate is formed
Quantification	Extract of the hollyhock	2.2.27 TLC	Qualitative reaction to atropine. the spots obtainedshould be at the level of the spots of the comparison solution of the standard pharmacopoeial sample
	Magnesium oxide light	2.5.11 Complexometry	99,1 % (98,0-100,5 %)
	Sodium bicarbonate	Titration	99,7 % (99,0-101,0 %)
	Camphor	2.2.28 TCC Impurities	100,0 %
	Ascorbic acid	Titration	99,5 % (99,0-100,5 %)
	Extract of the hollyhock	2.2.27 TLC	+Quantification in terms of hyoscyamine

1	2	3	4
Quantification	Extract of the hollyhock	2.2.27 TLC	Qualitative reaction to atropine. the spots obtainedshould be at the level of the spots of the comparison solution of the standard pharmacopoeial sample
	Magnesium oxide light	2.5.11 Complexometry	99,1 % (98,0-100,5 %)
	Sodium bicarbonate	Titration	99,7 % (99,0-101,0 %)
	Camphor	2.2.28 TCC Impurities	100,0 %
	Ascorbic acid	Titration	99,5 % (99,0-100,5 %)
	Extract of the hollyhock	2.2.27 TLC	+Quantification in terms of hyoscyamine

Table 3.5 **Results of studying the stability of powder samples for 6 months.**

Indicator.	**Sample**	**Results during storage**					
		1 month.	**2 months.**	**3 months.**	**4 months.**	**5 months.**	**6 months.**
1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Appearance	1a	+	+	+	+	+	+
	1b	+	+	+	+	+	+
	1c	+	+	+	+	+	+
	1d	+	+	+	+	+	+
	2a	+	+	+	+	+	+
	2b	+	+	+	+	+	+
	2c	+	+	+	+	+	+
	2d	+	+	+	+	+	+
	3a	+	+	+	+	+	+
	3b	+	+	+	+	-	-
	3c	+	+	+	+	+	+
	3d	+	+	+	+	-	-
	4a	+	+	+	+	+	+
	4b	+	+	+	+	-	-
	4c	+	+	+	+	+	+
	4d	+	+	+	+	-	-
	5a	+	+	+	+	+	+
	5b	+	+	+	+	-	-
	5c	+	+	+	+	+	+
	5d	+	+	+	+	-	-

1	2	3	4	5	6	7	8
	1a	+	+	+	+	+	+
	1b	+	+	+	+	+	+
	1c	+	+	+	+	+	+
	1d	+	+	+	+	+	+
	2a	+	+	+	+	+	+
	2b	+	+	+	+	+	+
	2c	+	+	+	+	+	+
	2d	+	+	+	+	+	+
	3a	+	+	+	+	+	+
Averege weight	3b	+	+	+	+	-	-
	3c	+	+	+	+	+	+
	3d	+	+	+	+	-	-
	4a	+	+	+	+	+	+
	4b	+	+	+	+	+	+
	4c	+	+	+	+	+	+
	4d	+	+	+	+	+	+
	5a	+	+	+	+	+	+
	5b	+	+	+	+	+	+
	5c	+	+	+	+	+	+
	5d	+	+	+	+	+	+

1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Weight Loss during drying	1a	+	+	+	+	+	+
	1b	+	+	+	+	+	+
	1c	+	+	+	+	+	+
	1d	+	+	+	+	+	+
	2a	+	+	+	+	+	+
	2b	+	+	+	+	+	+
	2c	+	+	+	+	+	+
	2d	+	+	+	+	+	+
	3a	//	//	//	//	//	//
	3b	//	//	//	//	//	//
	3c	//	//	//	//	//	//
	3d	//	//	//	//	//	//
	4a	+	+	+	+	+	+
	4b	+	+	+	+	+	+
	4c	+	+	+	+	+	+
	4d	+	+	+	+	+	+
	5a	+	+	+	+	+	+
	5b	+	+	+	+	+	+
	5c	+	+	+	+	+	+
	5d	+	+	+	+	+	+

1	2	3	4	5	6	7	8
identification	1a	+	+	+	+	+	+
	1b	+	+	+	+	+	+
	1c	+	+	+	+	+	+
	1d	+	+	+	+	+	+
	2a	+	+	+	+	+	+
	2b	+	+	+	+	+	+
	2c	+	+	+	+	+	+
	2d	+	+	+	+	+	+
	3a	+	+	+	+	+	+
	3b	+	+	+	+	+	+
	3c	+	+	+	+	+	+
	3d	+	+	+	+	+	+
	4a	+	+	+	+	+	+
	4b	+	+	+	+	+	+
	4c	+	+	+	+	+	+
	4d	+	+	+	+	+	+
	5a	+	+	+	+	+	+
	5b	+	+	+	+	+	+
	5c	+	+	+	+	+	+
	5d	+	+	+	+	+	+

1	2	3	4	5	6	7	8
Quantification	1a	+	+	+	+	+	+
	1b	+	+	+	+	+	+
	1c	+	+	+	+	+	+
	1d	+	+	+	+	+	+
	2a	+	+	+	+	+	+
	2b	+	+	+	+	+	+
	2c	+	+	+	+	+	+
	2d	+	+	+	+	+	+
	3a	+	+	+	+	+	+
	3b	+	+	+	+	-	-
	3c	+	+	+	+	+	+
	3d	+	+	+	+	-	-
	4a	+	+	+	+	+	+
	4b	+	+	+	+	-	-
	4c	+	+	+	+	+	+
	4d	+	+	+	+	-	-
	5a	+	+	+	+	+	+
	5b	+	+	+	+	-	-
	5c	+	+	+	+	+	+
	5d	+	+	+	+	-	-

According to the indicator "Average weight" during the first 4 months of storage, all samples showed a result that meets the requirements of the SPS. At 5 months of storage, camphor samples (3b, 3d) had inadequate results, as a partial transition of the powder to a liquid state was observed.

According to the indicator "Loss in weight during drying", samples 1a-1d, 2a-2d, 4a-4d showed good results. For samples of camphor (3a, 3b, 3c, 3d), the study was not carried out due to the high volatility of the powder.

In terms of the "Identification" indicator, the tested samples (1a-1d, 2a-2d, 3a-3d, 4a-4d) showed the proper result.

According to the indicator "Quantitative determination" during the first 4 months of storage, all samples showed a result that meets the requirements of the SPS. At the 5th month of storage, camphor samples (3b, 3d) had inadequate results, as a partial transition of the powder to a liquid state was observed.

Thus, the best quality indicators throughout the entire shelf life are those of sachets made of Foilbond and Transofoil, which are actually composite sachets with an inner layer made of aluminum foil and an outer layer made of paper (Foilbond) or plastic film (Transofoil).

When applying the labeling, it was found that Transofoil is more convenient: the labeling is easy to apply and does not erase, while the Foilbond paper coating can lose its pleasant consumer characteristics during long-term storage.

Thus, Transofoil sachets are the most convenient for long-term storage of pharmacy powders.

Conclusions to Chapter 3

1. Driven by the rising popularity of OTC drugs and the benefits of lower packaging costs, customizable designs, and space efficiency, the North American sachet packaging market for pharmaceuticals is thriving, with the US leading the way. While competition from stick packs with lower production costs exists, innovation in areas like moisture-control laminates is propelling the market forward. The COVID-19 pandemic further accelerated growth due to stockpiling of essentials, increased self-medication, and a focus on preventive healthcare. Key players like Amcor and Ahlstrom-Munksjo are capitalizing on this trend.

2. The quality study of 20 series of samples of 5 types of APIs (magnesium oxide, camphor, sodium bicarbonate, ascorbic acid, and lily extract) in sachets made of 4 types of materials (Foilbond, Transobond, Transofoil, Transoflow), which were stored for 6 months, was carried out according to such quality indicators as appearance, average weight, percentage of moisture, identification, and quantification. It was found that sachets made of Foilbond and Transofoil material had the best quality indicators throughout the entire storage period. When applyingthe labeling, it was found that Transofoil is more convenient: the labeling is easy toapply and does not erase, while the Foilbond paper coating may lose its pleasant consumer characteristics during long-term storage. Thus, Transofoil sachets were found to be the most convenient for long-term storage of pharmacy powders.

GENERAL CONCLUSIONS

1. The evolution and main links of the historical process of development and formation of solid medicinal forms are described. The history of the development of containers made of porcelain, earthenware and glass is described. The evolution of the packaging material of pharmaceutical powders from the use of classic capsules as primary packaging and paper bags and cans as secondary packaging to sachets of various types of materials that can combine primary and secondary packaging has been studied.

2. The characteristics of the research objects (magnesium oxide, sodium bicarbonate, camphor, ascorbic acid, belladonna extract) used in the experimental part are given. The methods of conducting economic, physico-chemical, pharmacotechnological tests, which were used in studying the influence of packaging material on the stability of powders during storage, are characterized.

3. The pharmaceutical market of medicinal products presented to the market of Ukraine in the form of sachets was studied. It was established that among the 5 medicinal products there are both domestic (40.0%) and foreign (60.0%) products. The analysis showed that the sachet as a form of packaging is suitable for a large number of medicinal products with different pharmacological and physicochemical properties.

4. Quality research of 20 series of samples of 5 types of API (light magnesium oxide, camphor, sodium bicarbonate, ascorbic acid, beauty extract) in sachets made of material of 4 types (Foilbond, Transobond, Transofoil, Transoflow), which were stored for 6 months ., was carried out according to such quality indicators as appearance, average weight, percentage of moisture, identification and quantification. Foilbond and Transofoil sachets have been found to have the best quality throughout the entire shelf life. When applying the marking, it was found that Transofoil is more convenient: the marking is applied easily, does not rub off, while the Foilbond paper coating can lose pleasant consumer characteristics during long-term storage. Therefore, the most convenient for long-term storage of pharmacy powders is a sachet made of Transofoil material.

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