WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 12, Issue 21, 200-214. Review Article ISSN 2277– 7105

# THE TRUTH ABOUT EXPIRED DRUGS: AN IN-DEPTH REVIEW

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Article Received on
05 October 2023,

Revised on 25 October 2023,
Accepted on 15 Nov. 2023

DOI: 10.20959/wjpr202321-30355

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## ABSTRACT

Drug expiration is the specific date at which a medication may no longer be considered safe for consumption. The World Health Organisation (WHO) recommends that each pharmaceutical product be accompanied by a package leaflet that provides comprehensive information on various aspects, including indications, potential adverse effects, possible interactions, and the expiry date. Since 1979, the Food and Drug Administration (FDA) has required pharmaceutical producers to include expiration dates on all pharmaceutical products. Research suggests that numerous medications can maintain 90% of their potency for a minimum of five years following the indicated expiration date, and in some cases, even beyond that timeframe. Management of expired pharmaceuticals can be achieved through enhanced inventory management, patient education, and return programs. Proper disposal of expired medications is crucial to prevent potential harm to individuals and the environment. Community pharmacists can play a significant role in managing and providing proper guidance on the appropriate disposal of unwanted and expired medications. Raising awareness on the appropriate disposal of unwanted and expired pharmaceuticals is a shared responsibility between the government, pharmacists, and the pharmaceutical industry.

**KEYWORDS:** Expired drugs, Expiry date, FDA, WHO, Drugs.

## INTRODUCTION

The term "drug expiration" refers to the specific date at which medicine may no longer be considered safe for consumption in its manufactured state. The determination of a drug's shelf life can be ascertained by locating the expiration date imprinted on the pharmaceutical

container.[1] Following the initial opening of the container, the efficacy of most medications, excluding specific drugs such as nitro-glycerine, insulin, epinephrine, and tetracycline, remains at a minimum of 70-80% of their original potency for a duration of 1-2 years beyond the expiration date, provided they are stored under suitable conditions.[2] The expiration date of a drug is determined based on the product type, either following the manufacturing process or subsequent to the dispensing of the medication. However, it should be noted that the rate of deterioration for drugs is not universally consistent, as different drugs may degrade at varying rates over time.[3] Medicines, on the other hand, can be classified into several synthetic or formulated categories, each with its own designated shelf life. According to the World Health Organisation (WHO), it is recommended that each pharmaceutical product be accompanied by a package leaflet that provides comprehensive information on several aspects, including the indications of the medication, potential bad effects, possible interactions, and the expiry date.[4] Since 1979, pharmaceutical producers have been required by the Food and Drug Administration (FDA) to include expiration dates on all pharmaceutical products.[5] It is possible for drugs that have exceeded their expiration date to retain their efficacy and potency. The potency that has been appropriately labelled will retain its activity until the specified expiration date, which is the sole assurance provided.[6] Ongoing research suggests that numerous medications can maintain 90% of their potency for a minimum of five years following the indicated expiration date, and in some cases, even beyond that timeframe. This preservation is observed when the drugs are stored in optimal settings.[7] A considerable proportion of medications retain a substantial level of their initial efficacy even a decade beyond their expiration date. In the majority of instances involving pharmaceutical items, the expiration date serves as an indicator of product quality. Following expiration, contamination may occur, evidenced by elevated levels of microbiological index. Additionally, the presence of excessive moisture content can also render such medications unfit for use.[8]

The objective of this review is to enhance understanding regarding medication expiration dates and to ensure the protection of patients from potentially ineffective or harmful treatment. Additionally, it aims to align healthcare practises with regulatory standards, minimise unnecessary waste, and optimise the management of pharmaceutical resources. Through a comprehensive exploration of this topic, it is possible to equip healthcare professionals, patients, and policymakers with the necessary knowledge to make well-informed decisions. This knowledge can facilitate the promotion of best practises in the

storage and utilisation of medicines, as well as encourage further research into the practical implications of expiration dates. Ultimately, these efforts can contribute to the development of a healthcare system that is both safer and more efficient.

**History of expiration dates**

Prior to 1979, the inclusion of expiration dates on pharmaceutical products was not obligatory for drug manufacturers. According to a regulation implemented by the U.S. Food and Drug Administration (FDA) in 1979, it is mandatory for all pharmaceutical manufacturers to include essential information on their product labels. The enactment of this legislation marked a notable change in societal attitudes towards the importance of medicine expiration dates. A study was done by the Food and Drug Administration (FDA) under the guidance of the military in order to get further insights into the topic of medicine expiration dates. This study was prompted by the military's need to address the challenge of periodically renewing and disposing of its costly and extensive inventory of drugs.[9]

In accordance with the findings, the Food and Drug Administration (FDA) conducted an analysis on a substantial number of both prescription and over-the-counter pharmaceuticals. The results indicated that almost 90 percent of the expired drugs remained safe and maintained their efficacy. Notably, the oldest medication included in the study had expired 15 years prior to the time of testing. The study highlighted that the indicated expiration date does not necessarily correspond to the point at which the medicine loses its efficacy or becomes dangerous for consumption. The information was published in a reputable news source, the Wall Street Journal, on March 29, 2000, as reported by Laurie P. Cohen.[10] Currently, there exists a collaborative initiative between the Department of Defence and the Food and Drug Administration (FDA) in the United States, referred to as the "Shelf Life Extension Programme" (SLEP). The primary objective of this programme is to mitigate expenses associated with replacing pharmaceuticals that have expiration dates by prolonging their efficacy beyond the original date specified by the manufacturer. The SLEP, which was initiated in 1986, commenced offering online services in 2005.[11] The article titled "Extending Shelf Life Just Makes Sense" published in Mayo Clinic Proceedings in 2015 proposed the idea of mandating pharmaceutical companies to establish an initial expiration date for drugs, which would subsequently be revised based on extensive long-term testing.[12] An alternative approach would involve the involvement of an autonomous entity to conduct testing, similar to the FDA extension programme. Alternatively, the data generated from the

extension programme might be utilised to assess the efficacy of appropriately maintained drugs.[13]

**Significance of expiry date written on drugs**

According to legal regulations, pharmaceutical companies are obligated to put an expiration date on their drug items. The specified date denotes the point at which the manufacturer can provide assurance of the medication's complete efficacy and safety. Potency refers to the inherent strength of a pharmaceutical substance at a specific dosage, which determines its ability to produce a desired therapeutic effect.[14] In the case of medications such as warfarin, a blood thinner used for preventing blood clots, or anti-seizure drugs like dilantin or phenobarbital, it is crucial to ensure that the medication maintains its maximum efficacy in order to mitigate the potential adverse consequences associated with medication ineffectiveness.[15]

As per the study conducted by Dr. Rohr of New York University Langone Joan H. Tisch Center for Women's Health, there exists no scientific substantiation to indicate that expired pharmaceuticals possess the potential to induce toxicity or elicit adverse health effects similar to the manner in which spoiled food can. It is probable that the medicine will experience a decrease in potency subsequent to its expiration date; however, the extent of potency reduction within a defined period beyond the expiration date remains uncertain. The expiration date assigned to creams signifies the manufacturer's assurance that the product will retain a potency level of at least 90% until that specified date.[16]

The reduction in potency can vary, ranging from as little as a 5% decrease to a 50% decrease in potency. However, it is worth noting that many drugs may still retain a reasonably high level of potency even after a period of five to ten years following their expiration. However, in certain instances, it has been documented that certain antibiotics undergo a chemical transformation into a novel state subsequent to their expiration date, potentially resulting in adverse effects.[17] The findings presented in this study were published by Frimpter et al. in the Journal of the American Medical Association in 1963. The study investigated the effects of expired tetracycline on kidney function, and the authors reported the occurrence of adverse side effects. However, it is important to note that the observations and conclusions made by the authors have been subject to debate and disagreement among other medical researchers.[18]

Solid dosage forms, such as tablets and capsules, have a higher degree of stability beyond their designated expiration date. Pharmaceutical substances that are present in a liquid form or as a reconstituted suspension, and necessitate refrigeration for storage (e.g., amoxicillin suspension), may exhibit diminished potency if utilised after their expiration date. The decrease in effectiveness can pose a significant health risk, particularly in the context of utilising antibiotics for the treatment of infections. Furthermore, the phenomenon of antibiotic resistance might manifest in the presence of drugs that possess suboptimal potency. It is recommended to discard pharmaceuticals that are in solution, particularly injectable drugs, if the product undergoes precipitation or exhibits cloudiness or discoloration.[19]

**Potency and Efficacy in relation to expired drugs**

The efficacy of medication diminishes progressively from the time of its production. The occurrence of this process does not exhibit any form of spontaneity subsequent to the expiration date. The potency and efficacy of expired medications may not necessarily be compromised. The designated expiration date serves as a guarantee that the indicated potency of the product will be effective until that specified date.[20] Current research indicates that when preserved under ideal conditions, numerous pharmaceuticals maintain approximately 90% of their efficacy for a minimum of five years beyond the designated expiration date, and occasionally even longer. Pharmaceuticals sometimes maintain a considerable level of their initial efficacy even a decade beyond their expiration date.[21]

Psychological factors can exert an influence on the effectiveness of medications. Consequently, it is crucial to emphasise that the stability of medication quality and appropriateness is substantiated by the expiration date. Although the American Medical Association and the Food and Drug Administration currently do not provide guidelines for the administration of expired pharmaceuticals, it is important to engage in a discussion regarding this matter in order to gain insight into the potential of certain expired medications and to encourage further research.[22]

**Shelf-life extension program (Slep)**

The Shelf-Life Extension Programme (SLEP), conducted by the Food and Drug Administration (FDA) on behalf of the Department of Defence, offers the most compelling data about the continued efficacy of pharmaceuticals beyond their expiration date. The primary objective of the SLEP programme was to mitigate pharmaceutical expenses incurred by the military.[23] According to the findings of the Shelf-Life Extension Programme (SLEP),

it has been revealed that about 88% of a total of 122 distinct pharmaceuticals, when maintained under optimal conditions, are eligible for an extension of their expiration dates by more than one year. The average extension period observed is approximately 66 months, with the maximum extension period reaching up to 278 months. Certain drugs possess a limited therapeutic index, whereby even slight reductions in pharmacological activity can lead to significant repercussions for patients. Monoclonal antibodies should be included in this group and it is not advisable to utilise these pharmaceutical substances beyond their designated expiration date.[24]

**Table 1: A comparison of essential Drugs and Their average extension time.[24]**

| Drug types | Drug generic name | Average extension time in months (range) |
|---|---|---|
| Analgesics | Morphine sulphate (injectable) | 89 (35-119) |
| | Fentanyl citrate (injectable) | 84 (70-96) |
| | Ketamine HCl (injectable) | 64 (42-87) |
| | Naproxen (tablets) | 52 (46-62) |
| Antibiotics | Amoxicillin sodium (tablets) | 23 (22-23) |
| | Ciprofloxacin (tablets) | 55 (12-142) |
| | Doxycycline hyclate (capsules) | 50 (37-66) |
| | Cephalexin (capsules) | 57 (28-135) |
| | Ceftriaxone (powder) | 60 (44-69) |
| Intravenous fluids | Sodium chloride | 50 (12-113) |
| | Dextrose (5%) | 65 (13-128) |
| | Sodium lactate | 53 (20-87) |

**Health hazard associated with expired drugs**

The potential hazards associated with the existence of unused and expired pharmaceuticals in cabinets and cupboards pose risks to human health, as well as to the environment and wildlife. The issue of abandoned pharmaceuticals contaminating streams and drinking water received significant attention at both national and international levels, capturing the interest of the general public, legislators, and regulatory bodies.[25] The pain-relieving chemical diclofenac, which is often used, has been found to cause renal failure in vultures when they consume the remains of cows that have been treated with this medication.[26] It is advised against ingesting pills that exhibit signs of discoloration, powdery texture, or unpleasant odour. Similarly, liquids that have cloudiness or film-like appearance, as well as cream tubes that are hardened or fractured, should be avoided.[27]

The World Health Organisation (WHO) has identified the consumption of low-quality antibiotics, which encompasses the use of expired and counterfeit medications, as a

significant challenge in the progression of antimicrobial resistance within low-income and middle-income countries (LICs/LMICs).[28] In 2014, the Pan African Medical Journal published a study that examined the ex vivo impact of expired paediatric antibiotics on samples of infantile diarrheagenic bacteria. The findings of this investigation revealed a notable escalation in the prevalence of antibiotic resistance among cultivated bacteria towards expired antibiotics. Notably, many strains exhibited complete resistance, reaching up to 100%, to the expired antibiotics in comparison to their non-expired counterparts. Nevertheless, the effectiveness of paediatric preparations was considerably constrained due to their liquid form, which renders them more vulnerable to degradation due to the relatively short lifespan of their preservatives, in contrast to the protective coating often present on tablets and pills.[29]

According to a report by the American Society of Tropical Medicine and Hygiene in 2015, it was estimated that approximately 122,000 children below the age of five in sub-Saharan Africa lost their lives as a result of consuming substandard antimalarial drugs. These drugs, along with antibiotics, are the most sought-after medications and are particularly susceptible to issues such as expiration or counterfeiting. Certain drugs, such as insulin and certain liquid antibiotics, exhibit rapid degradation and should not be utilised beyond their designated expiry date.[30]

**Financial implications**

The financial ramifications associated with the expiration of pharmaceuticals are substantial, encompassing both individual and societal domains.

**For individuals**

1. **Medication replacement:** In cases where medications have reached their expiration date and necessitate replacement, patients are required to bear the entire financial burden associated with acquiring the new pharmaceutical product. The financial implications of this circumstance can be particularly costly, particularly for individuals who are prescribed multiple medications or who possess constrained financial resources.[31]

2. **Adverse effects:** The cost associated with the management of adverse effects resulting from the utilisation of expired medications can be considerable. These pharmaceutical products, once expired, may exhibit diminished efficacy or potentially induce unfavourable reactions within the patient. In the event that a patient encounters untoward

consequences as a result of the ingestion of expired pharmaceuticals, it may become necessary for them to pursue medical intervention, thereby potentially expanding their financial burden.[32]

**For society**

3. **Lost revenue for pharmaceutical companies:** The loss of revenue incurred by pharmaceutical companies arises from the disposal of expired medications, thereby losing the potential earnings associated with the production of said pharmaceuticals. The potential consequence of this loss in revenue may manifest in an escalation of prices for alternative pharmaceuticals.[33]

4. **Increased costs for healthcare systems:** The escalating expenses incurred by healthcare systems are primarily attributed to the financial burden associated with the proper disposal of expired medications. The financial burden associated with this matter can be quite substantial, particularly in regions characterised by lower and middle socioeconomic statuses.[34]

5. **Environmental costs:** Improper disposal of expired medications may result in environmental pollution. The aforementioned phenomenon has the potential to induce adverse ecological consequences and pose significant health risks to both human beings and fauna.[35]

According to estimations provided by the World Health Organisation (WHO), the financial burden incurred due to the expiration of pharmaceuticals on a global scale amount to billions of dollars annually. A recent publication in the esteemed journal BMC Health Services Research has shed light on a significant concern pertaining to the Ethiopian healthcare system. The study in question has revealed that the financial burden associated with expired medicines in Ethiopia amounts to a staggering 4% of the nation's annual healthcare budget. This finding underscores the pressing need for effective strategies to mitigate the economic implications of medication wastage in this region.[36]

**Strategies for management of expired drugs**

There exist a multitude of measures that can be undertaken to mitigate the occurrence of expired pharmaceuticals, encompassing the following:

- **Enhanced inventory management:** It is imperative for healthcare providers and pharmacies to optimise their inventory management systems in order to mitigate the accumulation of expired medication within their facilities.[37]

- **Patient education:** It is imperative to provide patients with comprehensive knowledge regarding the significance of diligently inspecting the expiration dates of their prescribed medications and appropriately discarding any expired medications.[38]

- **Pharmacies and Healthcare providers** may provide return programmes for expired medications. These programmes facilitate the opportunity for patients to return medications that have reached their expiration date for appropriate disposal.[39]

By implementing the following measures, we can effectively mitigate the economic and ecological burdens associated with the disposal of expired pharmaceuticals.

**Guidelines for the proper disposal of expired drugs**

The careful disposal of expired medications is vital to prevent any potential harm to individuals and the environment. The degradation process might result in a decrease in the potency of pharmaceutical drugs. Physical alterations can potentially result in diminished absorption, hence compromising the efficacy of the products. The liability of a pharmaceutical manufacturer for any adverse consequences resulting from their product is contingent upon two factors: the product's shelf life and adherence to the manufacturer's specified transportation and storage conditions. The demand for cost-effective management and techniques arises from limits in funding for the disposal of waste medicines.[40] The following are the recommended guidelines for the safe disposal of expired drugs:

**Table 2: Summary of pharmaceutical Categories and Disposal methods In and After emergencies.[40]**

| Category | Disposal methods | Comments |
|---|---|---|
| Solids | Landfill | No more than 1% of the daily municipal waste should be disposed of daily in an untreated form (non-immobilized) to a landfill |
| Semi-solids | Waste encapsulation | |
| Powders | Waste inertization | |
| | Medium and high temperature incineration (Cement kiln incinerator) | |

| | | |
|---|---|---|
| Liquids | Sewer | Antineoplastics not to sewer |
| | high temperature incineration (Cement kiln incinerator) | |
| Ampoules | Crush ampoules and flush diluted fluid to sewer | Antineoplastics not to sewer |
| Anti-ineffective drugs | Waste encapsulation | Liquid antibiotics may be diluted with water, left to stand for several weeks and discharged to a sewer |
| | Waste inertization | |
| | Medium and high temperature incineration (Cement kiln incinerator) | |
| Antineoplastics | Return to donor or manufacturer | Not to landfill unless encapsulated |
| | Waste encapsulation | Not to sewer |
| | Waste inertization | No medium temperature incineration |
| | Medium and high temperature incineration (Cement kiln incinerator) | |
| Controlled drugs | Waste encapsulation | Not to landfill unless encapsulated |
| | | |
| | Waste inertization | |
| | Medium and high temperature incineration (Cement kiln incinerator) | |
| Aerosol canisters | Landfill, Waste encapsulation | Not to be burnt, may explode |
| Disinfectants | Use To sewer or fast-flowing watercourse: small quantities of diluted disinfectants (max. 50 litres per day under supervision) | No undiluted disinfectants to sewers or water courses<br>Maximum 50 litres per day diluted to sewer or fast-flowing watercourse<br>No disinfectants at all to slow moving or stagnant watercourses |
| PVC plastic, glass | Landfill | Not for burning in open containers |
| Paper, cardboard | Recycle, burn, landfill | |

The expired medicines should not be flushed down the toilet unless specifically instructed to do so because of the earlier reported risk of the resistant bacteria in the aeration tanks of sewage treatment plants by the antibiotic substances present. The exceptions to the rule are narcotics and controlled substances, which are often flushed to prevent unintentional use, overdose and illegal abuse.[41]

**Role of pharmacist**

Community pharmacists have the potential to play a significant role in the management and provision of proper guidance and care to the community about the appropriate and standardised disposal practises of unwanted and expired medications. The government's prioritisation of the provision of free medications in public hospitals is of considerable importance, as research has indicated a correlation between the availability of free prescriptions and increased medication wastage.[42] The findings of this study hold considerable importance in the context of formulating national policies pertaining to medicine supplies and addressing the issue of drug wastage. The cultivation of awareness on the appropriate disposal of unwanted and expired pharmaceuticals is a shared responsibility of governmental bodies, pharmacists, and pharmaceutical companies.[43]

## CONCLUSION

The expiration dates of medications serve as an indication of the period during which they are certain to exhibit optimal effectiveness. Several pharmaceutical substances, when maintained appropriately, retain their efficacy and safety for consumption even after their designated expiration date. Several literatures highlight the significance of nitro-glycerine, insulin, epinephrine, and tetracycline, emphasising the importance of refraining from using these substances beyond their expiration dates. Nevertheless, adhering to storage protocols and disposing of pharmaceuticals that exhibit questionable characteristics is of utmost importance. The inappropriate disposal of unwanted and expired pharmaceuticals poses a potential hazard and has the capacity to cause harm to both human beings, the environment, and wildlife. Returning unwanted and expired drugs to medical stores for proper disposal is considered a commendable practise. The responsibility for raising awareness on the appropriate disposal of unwanted and expired pharmaceuticals lies with the government, pharmacists, and the pharmaceutical industry.

## ACKNOWLEDGEMENT

Putting together this review piece has been a labour of love and teamwork, and I'm very thankful to everyone who helped make it happen. I want to thank my co-author, from the bottom of my heart for their hard work, creativity, and friendship. We've worked together to make a story that I'm proud to tell you all. Thank you from the bottom of our hearts to the smart reviews whose comments have made our work better. Thank you for the helpful feedback that has made this piece better. Your knowledge has been a light to follow.

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