

From The Medical Letter on Drugs and Therapeutics

Drugs Past Their Expiration Date

Healthcare providers are often asked if drugs can be used past their expiration date. Because of legal restrictions and liability concerns, manufacturers do not sanction such use and usually do not even comment on the safety or effectiveness of their products beyond the date on the label. Since our last publication on this subject,¹ more data have become available.

Safety

There are no published reports of human toxicity due to ingestion, injection, or topical application of a current drug formulation after its expiration date. Renal tubular damage has been reported with use of degraded tetracycline in a formulation that is no longer available.²

The Expiration Date

The manufacturer's expiration date is based on the stability of the drug in the original sealed container. The date does not necessarily mean that the drug was found to be unstable after a longer period; it only means that real-time data or extrapolations from accelerated degradation studies indicate that the drug in the closed container will still be stable at that date. Most drug products have a labeled shelf life of 1-5 years, but once the original container is opened, the expiration date on that container no longer applies.

Stability

Data from the US Department of Defense/FDA Shelf Life Extension Program, which tests the stability of drug products past their expiration date, have shown that 2650 of 3005 lots (~88%) of 122 different products stored in their unopened original containers remained stable for an average of 66 months after their expiration date.³ Of these, 312 lots (~12%) remained stable for >4 years after the expiration date. Failure on the basis of potency, pH, water content, dissolution, physical appearance, or presence of impurities occurred in 479 lots (~18%), but none failed within 1 year. Potassium iodide, which has been extensively stockpiled for use in a radiation emergency, has shown no significant degradation over many years.⁴

Heat, Humidity, and Long-Term Storage

Storage in high heat and/or humidity can accelerate the degradation of some drug formulations, but in one study, captopril tablets, theophylline tablets (Theo-Dur, and others), and cefoxitin

sodium powder for injection (Mefoxin, and others), stored at 40°C and 75% relative humidity, remained stable for 1.5-9 years beyond their expiration dates.⁵ In another study, theophylline retained 90% of its potency 30 years past its expiration date.⁶ A study of eight products that had been stored in their unopened original containers for 28-40 years past expiration found that 12 of 14 active ingredients had retained $\geq 90\%$ of their original potency; aspirin retained <5% of its potency and amphetamine <60%.⁷

Liquid Drugs

Solutions and suspensions are generally less stable than solid dosage forms, but in one report, four outdated samples of atropine solution (three up to 12 years past expiration and one >50 years past expiration) were all found to contain significant amounts of the drug.⁸ Drugs in solution that have become cloudy or discolored or show signs of precipitation, particularly injectables, should not be used. Suspensions are especially susceptible to freezing. Limiting factors with ophthalmic drugs include evaporation of the solvent and the continued ability of the preservative to inhibit microbial growth.⁹

Epinephrine solutions in EpiPen auto-injectors may lose potency after the expiration date. In a study of 34 pens that had expired 1-90 months previously, the decrease in epinephrine content was proportional to the number of months past the expiration date.¹⁰ One study found that pens 3-36 months past their expiration dates contained 84.2-101.5% of the labeled dose,¹¹ but a study of pens stored in EMS vehicles that had expired 1-11 years previously found that only 12.6%-31.3% of the labeled dose remained.¹² No data are available on other epinephrine auto-injectors such as Auvi-Q.¹³

Conclusions

When no suitable alternative is available, outdated drugs may be effective. How much potency they retain varies with the drug, the lot, the preservatives (if any), and the storage conditions, especially heat and humidity; many solid dosage formulations stored under reasonable conditions in their original unopened containers retain $\geq 90\%$ of their potency for at least 5 years after the expiration date on the label, and sometimes much longer. Solutions and suspensions are generally less stable. There are no reports of toxicity from degradation products of currently available drugs.

ARTICLE INFORMATION

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