PHOTOSTABILITY CHALLENGES AND STABILIZATION STRATEGIES IN PHARMACEUTICAL DOSAGE FORMS

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ABSTRACT

Photostability is a critical quality attribute in pharmaceutical dosage forms, as exposure to light can trigger photodegradation of active pharmaceutical ingredients (APIs), leading to reduced potency, altered pharmacological activity, or the formation of toxic by-products. Many drugs, including non-steroidal anti-inflammatory agents, antihypertensives, and antibiotics, are highly susceptible to light-induced degradation due to their aromatic, halogenated, or conjugated molecular structures. Regulatory authorities, such as the International Council for Harmonisation (ICH), mandate photostability testing to ensure drug safety and efficacy throughout shelf life. Stabilization strategies have therefore become an essential component of formulation design. Approaches include the incorporation of UV absorbers and antioxidants, selection of protective packaging materials, complexation with cyclodextrins, and the development of film-forming biodegradable polymers that act as physical light barriers. Advanced techniques such as nanoparticle encapsulation, liposomal carriers, and polymeric coatings further enhance photoprotection while maintaining drug release profiles. This review highlights the underlying mechanisms of drug photodegradation, the regulatory requirements for photostability studies, and the current formulation strategies employed to minimize photo liability. Emphasis is placed on the integration of eco-friendly, biodegradable packaging and polymer-based films as emerging solutions to ensure drug stability while aligning with sustainable pharmaceutical development.

Keywords: *Photostability, International Council for Harmonisation, Photodegradation*

INTRODUCTION

Pharmaceutical formulation aims to create a delivery system that safely and effectively administers the active ingredient to the body in a consistent and convenient manner. Excipients are used to enhance various properties of the active ingredient, including solubility, stability, suspension, texture, preservation, emulsification, dissolution rate, compressibility, and flavour. For the final product to be safe, stable, and effective, it's crucial that excipients are compatible with the active ingredient. [1,2] Many drugs are vulnerable to light, which can cause them to break down or lose potency during production, storage, or use. [3] This can result in unwanted consequences, including: Loss or change of the active ingredient or excipients, Reduced drug effectiveness, Formation of unwanted by-products or other adverse effects on the product's quality and safety. [4]

Photostability refers to the impact of light on the stability of pharmaceutical substances and products. Light exposure can affect both the active ingredients and the final product or packaging, potentially altering their quality and efficacy. Essentially, photostability studies provides an understanding of how light (photons) influences the stability of pharmaceuticals.[5]

Photodegradation can cause visible changes like: Bleaching or discoloration, Cloudy appearance, Loss of viscosity, Precipitation of active ingredients, Changes in dissolution rate, etc., The impact varies depending on the compounds: Some drugs degrade slowly over weeks and others, like certain dihydropyridine derivatives (e.g., nifedipine), break down rapidly, with a half-life of just minutes. [6,7] Sunlight can trigger harmful reactions in certain drugs, leading to the formation of toxic byproducts or reactive oxygen species that can cause oxidative damage and potentially harm human tissues. Even brief or minimal exposure to light can be problematic, and the most significant consequence of this photodegradation is a loss of drug potency, making the medication less effective. [8,9]

To ensure the safety, efficacy, and quality of pharmaceuticals, it's crucial to test them for photodegradation. Key factors influencing photodegradation include - Light intensity and wavelength, pH levels, Ionic strength, Solvent properties, Viscosity, Humidity. The FDA adopted the ICH Q1B guideline in 1997, outlining a systematic approach to photostability testing for new drug substances and products. This includes testing:

1. The drug substance itself
2. The product in its packaging
3. The product in its marketed form

This guideline helps ensure pharmaceuticals can withstand light exposure and maintain their quality. [4,10]

For drug substances, photostability evaluation involves two key steps:

I. Forced degradation testing: This assesses the drug's overall sensitivity to light by exposing it to intense light in a transparent container.

II. Confirmatory testing: This determines the appropriate handling, storage, and shipping conditions to ensure the drug's stability. [11,12]

To protect light-sensitive formulations or compounds, precautions like protective packaging can minimize light exposure. The packaging choice depends on the specific wavelengths causing instability. If formulation modifications are needed to enhance shelf life, the impact of excipients and product presentation must be considered to ensure stability. [5]

Packaging in suitable containers can often protect light-sensitive drugs, but it's not the only solution. While plastic packaging is sometimes used, studies show it offers limited protection against radiation. Photodegradation risks vary depending on factors like: Formulation type (solid or liquid), Packaging material, Administration route and storage conditions. Each factor must be considered to ensure effective protection. [2]

To stabilize light-sensitive products, understanding the nature and extent of photodegradation is crucial. This review explores photostability challenges in formulations and discusses strategies to address them, helping to enhance product stability. [2]

PHOTODEGRADATION PROCESS

Photodegradation occurs through two mechanisms:

1. Direct reaction: When the drug absorbs radiation directly.
2. Indirect reaction: Involving other molecules or substances.

Photodegradation happens when the drug's absorption spectrum matches the radiation source's wavelength. [13]

Direct Reaction

In direct reaction, light-sensitive substances absorb light energy, forming intermediates that eventually convert to stable molecules.

When molecules absorb photons, they enter an excited singlet state, triggering transformations. This state can convert to an excited triplet state, leading to various reactions, including: Homolysis, Heterolysis, Photoionization, Direct reactions with the surrounding medium. These reactions occur due to the molecule's increased energy state. [4]

Indirect Reaction

In indirect reaction, excipients or intermediates absorb light energy and transfer it to the drug, causing degradation. This process can continue even without light (dark reaction). Indirect photodegradation of light-sensitive compounds can occur through:

1. Photosensitized degradation: A photosensitizer absorbs light, becomes excited, and transfers energy to the target compound, triggering degradation.
2. Photoinduced degradation: Intermediates formed during the photochemical process react with the target compound, causing decomposition.

The rate of photodegradation depends on the photosensitizer's activation level. [14]

Photochemical Reactions

Various photochemical reactions can occur, including:

1. Oxidation
2. Hydrolysis
3. Hydroxylation
4. Isomerization
5. Decarbonylation
6. Decarboxylation
7. N-dealkylation

Functional Groups Involved

Key functional groups susceptible to photodegradation include:

1. Carbonyl groups
2. Carbon-carbon double bonds
3. C-H bonds in alcohols, amines, and sulfides

Degradation Rate

The rate of degradation depends on the concentration of these functional groups and the solution's concentration. [15]

Factors affecting photodegradation

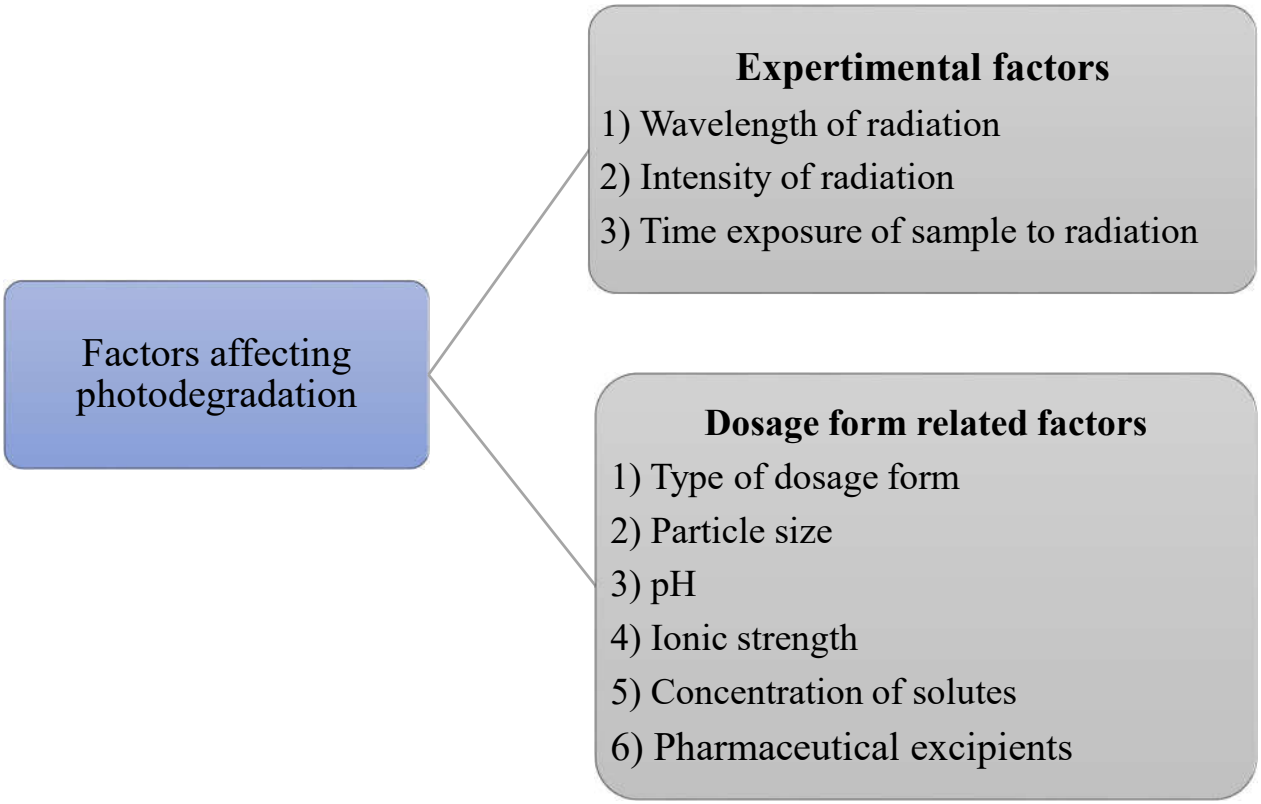

Fig.1 Factors affecting photodegradation

Photodegradation is influenced by factors like wavelength, intensity, and exposure time. Shorter wavelengths have higher energy, causing faster degradation, while higher intensity and longer exposure times also increase degradation. Photostability refers to the impact of light on pharmaceutical substances or products. Excipients play a crucial role, potentially acting as sensitizers, making compatibility studies between drugs and excipients essential before formulation. [16]

Light's Role in Photodegradation

Light is essential for photodegradation reactions, and variations in light sources affect wavelength, energy, and intensity. Sunlight's UV and visible light range (290-760 nm) can trigger degradation. High-intensity light with shorter wavelengths generates reactive intermediates, accelerating photodegradation and reducing the half-life of photosensitive molecules. Studies show that reducing light intensity can linearly increase the degradation half-life of photolabile compounds, such as tetracycline. [17]

Drug	Light intensity/type of radiation	Half-life or degradation rate (min)
Tetracycline	sunny noon cloudy noon overcast noon	5.87 10.98 19.04
Geldanamycin	1500±500 1x 3000±500 1x 4500±500 1x	268.00 120.00 67.00
Riboflavin	UV (240-366 nm) Visible (400-500 nm)	7.5 min 330 min
Chloroquine	UV (240 nm) Visible (600 nm)	Fast Slow

Table 1: The Effect of Different Light Intensities on the Photodegradation of Selected Drugs [2]

pH

The pH of an aqueous environment significantly impacts drug photodegradation, potentially promoting or inhibiting the process. Changes in pH can alter the rate of photolysis and the formation of intermediates and final products, which may in turn affect the environment's pH and accelerate degradation. For example, tetracycline, oxytetracycline, and chlortetracycline undergo TiO2-catalyzed photolysis in aqueous solutions, highlighting the importance of pH in photodegradation reactions.

The rate of photodegradation of tetracycline (TC), oxytetracycline (OTC), and chlortetracycline (CTC) with TiO2 is influenced by pH-dependent electrostatic interactions. At TiO2's isoelectric point (pH 6.8), where the surface charge is neutral, photolysis accelerates due to reduced electrostatic interactions. [18]

Drug	pH	Half-life (period/min)
Tetracycline	3.0 5.0 7.0	104.00 76.00 61.10
Oxytetracycline	3.0 5.0 7.0	72.10 58.20 39.10
Chlortetracycline	3.0 5.0 7.0	46.80 42.70 40.80
Oxazolidinone	4.9 6.2 11.0	16.17 15.07 16.67
Erythromycin and Roxithromyxcin	6.3 7.5 8.5	70.00 30.00 80.00

Table 2: The Effect of pH on the Photodegradation of Selected Drugs [2]

Concentration

The concentration of drugs or photosensitizers impacts photodegradation rates. Higher concentrations can: Increase degradation via reactive intermediates and chain reactions; Decrease degradation in the bulk due to limited light penetration. The lower concentrations often result in faster photodegradation rates. [19]

Even small amounts of photosensitizers can impact dosage form stability. For example, carbamazepine tablets turned yellow to orange upon UV exposure due to photodegradation of the drug's polymorphic form II, triggered by interaction with a photosensitizing excipient. [5]

Temperature

Temperature typically doesn't directly drive photodegradation reactions, which often occur at room temperature through photon absorption. However, as photodegradation progresses, released energy can increase the system's temperature, potentially accelerating the reaction. [4]

Water composition

The presence of ions and organic compounds in water significantly affects drug degradation. Ions like nitrates and nitrites, common in aquatic environments, generate hydroxyl

radicals upon photolysis, triggering oxidation and nitration reactions. Hydroxyl ions and radicals can also scavenge UV light, further influencing degradation processes. Most pharmaceutical products, except some solid oral dosage forms, typically use purified or deionized water during manufacturing. [20]

PHOTODEGRADATION OF PHARMACEUTICALS

Active pharmaceutical ingredient

Understanding a drug's photochemical degradation is crucial for developing effective photo stabilization strategies. Photochemical reactions can lead to loss of efficacy or adverse effects. For instance, ketoprofen's photodecarboxylation reaction forms a photoallergic compound (3-ethylbenzophenone), causing skin reactions like erythema, edema and pigmentation. Ketoprofen gels were removed from the Spanish and French markets in 2009 due to frequent photosensitivity reactions. Following a safety review, the European Medicines Agency reclassified ketoprofen from over-the-counter to prescription-only, citing concerns over its risk-benefit profile. [21]

Ascorbic acid in topical creams is photo unstable, undergoing photooxidation to form dehydroascorbic acid and 2,3-diketogulonic acid. To enhance stability, it's often paired with a redox partner. [22]

Similarly, chlorpromazine, an antipsychotic, undergoes photooxidation in solution, forming a cation radical intermediate that ultimately yields chlorpromazine 5-sulfoxide, highlighting the need for photo stabilization strategies. [4]

Therapeutic group	Drugs
Central nervous system acting drugs	Neuroleptics: chlorpromazine, thioridazine, trifluoperazine, clozapine Antidepressants: amitriptyline, imipramine, fluoxetine, paroxetine Sedato-hypnotics: diazepam, alprazolam, chlordiazepoxide. Antiepileptics: carbamazepine, lamotrigine, phenytoin
Cardiovascular system acting agents	Antiarrythimics: amiodarone, quinidine Ca2+ channel blockers: nifedipine, amlodipine, diltiazem ACE inhibitors: ramipril, quinapril, enalapril Diuretics: furosemide, hydrochlorothiazide Statins: simvastatin, atorvastatin, pravastatin

Non-steroidal anti-inflammatory drugs	Ketoprofen, ibuprofen, naproxen, diclofenac, indomethacin, phenylbutazone
Antidiabetics	Glipizide, glyburide, glibenclamide, glimepiride
Antihistamines	Cyproheptadine, diphenhydramine, dimetindene, loratadine, cetirizine
Antipathogenic agents	Antibacterial agents: fluoroquinolones, tetracyclines, sulphonamides and trimethoprim, cefotaxime, ceftazidime, metronidazole Antifungals: voriconazole, itraconazole, terconazole, flucytosine, griseofulvin, bifonazole, fluconazole Anti-malaria agents: quinine, chloroquine, hydroxychloroquine Antivirals: efavirenz, saquinavir, acyclovir, ritonavir, zalcitabine
Antineoplastic agents	Vandetanib, imatinib, fluorouracil and structurally related substances (tegafur, capecitabin), paclitaxel, methotrexate, vinblastine, dacarbazine
Systemic dermatologic agents	Isotretinoin, methoxsalen, acitretin
Herbs	Hypericin, fluorocoumarin

Table 3: Drugs undergoing photosensitivity [23]

Polymer degradation

Polymer-based drug delivery systems can be compromised by polymer degradation, which affects product efficacy. Factors influencing degradation include:

1. Chromophore-containing impurities
2. Radiation intensity
3. Storage conditions
4. Presence of low molecular weight organic compounds

These factors can significantly impact the system's performance and stability.

The presence of chromophoric groups in polymers can lead to photo instability. For example, polystyrene discolorises when exposed to UV radiation. The combination of UV light and oxygen accelerates polymer degradation through photooxidation, which is influenced by the polymer chain structure and matrix rigidity. Energy transfer also plays a key role in initiating photooxidation, especially at high temperatures. Polymers like polystyrene, polyvinyl, polyethylene, and polyester are commonly used in drug delivery systems.

Fortunately, these polymers are generally photostable when exposed to light with wavelengths of 290 nm or less. [24,25]

Lipid degradation

Lipid-based drug delivery systems can be compromised by photodegradation, where lipids are directly damaged by photons or indirectly by photosensitizers. Key factors contributing to lipid peroxidation include:

1. High content of polyunsaturated fatty acids (PUFAs)
2. Chain length of the fatty acids

These factors can impact the quality and stability of the drug product. The extent of lipid peroxidation in drug formulations is influenced by the Intensity of ultraviolet (UV) light exposure and concentration of the light-sensitive drug. [4]

Nalidixic acid decreased the stability of DOPC (dioleoyl-phosphatidylcholine) liposomes by generating free radicals under UVB irradiation, affecting the entire phospholipid chain. In contrast, DPPC(α-l-dipalmitoyl phosphatidylcholine) liposomes showed no immediate thermodynamic changes with or without nalidixic acid. However, lipid peroxidation and unsaturation occurred, potentially leading to long-term destabilization of the liposomes. [26]

APPROACHES TO IMPROVE THE PHOTOSTABILITY OF DRUGS

Understanding the photochemistry of APIs and drug products is crucial for development. To protect drugs from light, two strategies are employed: external and internal protection. External protection involves using opaque containers, brown glass, aluminium foil wraps, or tablet coatings with UV absorbers and opacifiers like titanium dioxide to block light. Internal protection, on the other hand, incorporates additives like coloured dyes that competitively absorb causative wavelengths or quench photoreactions, helping to stabilize the drug. Cyclodextrins, acting as excited state quenchers, have been utilized to stabilize various drugs by mitigating photodegradation reactions. [19]

Vesicular carrier

Vesicular structures, such as liposomes (phospholipid-based vesicles) and niosomes (non-ionic surfactant-based vesicles), have been proposed as delivery systems to enhance the stability and efficacy of photosensitive drugs. Liposomes and niosomes have a hydrophobic core and hydrophilic shell, enabling them to encapsulate drug molecules in either the aqueous space or within the phospholipid bilayer, enhancing drug delivery. [27]

Encapsulating drugs in liposomes or niosomes can enhance their photostability. Examples include:

1. Tretinoin (TRA) showed retarded photodegradation when included in liposomes or niosomes.
2. Riboflavin showed increased photostability with neutral and negatively charged liposomes. [28]
3. Doxorubicin showed reduced photodegradation when encapsulated in polyethylene glycol-coated liposomes. These vesicular systems can protect photosensitive drugs from degradation. [29]

Lipid nanoparticles

Lipid-based nanoparticles (LBNs), including solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs), have emerged as effective systems for enhancing the photostability of light-sensitive drugs. [30]

Lipid-based nanoparticles (LBNs) enhance photoprotection by combining strengths with sun screening agents. For example, solid lipid nanoparticles (SLNs) loaded with dithranol in a gel formulation improved photostability by stabilizing the drug within the lipid matrix. [31]

Microspheres or microcapsules

In microsphere formulations, drugs are dissolved, dispersed, or absorbed within polymer carriers, creating a matrix that protects the drug from photodegradation through physical or chemical barriers.

Abamectin, a light-sensitive drug, can be protected from degradation by encapsulating it with zein, a corn-derived protein, which effectively retards oxidation and provides high light protection. [32]

Microcapsules made with methacrylic copolymers have enhanced the photostability of curcumin by shielding it from light-induced degradation, providing effective protection. [33]

Liquisolid system

Liquisolid systems are being explored as a promising approach to enhance photoprotection for photosensitive drugs, offering a potential alternative to traditional coating methods for improving drug stability. Silicon dioxide or its derivatives are key excipients in liquisolid systems, and their higher refractive index enables diffraction of light waves, contributing to enhanced photoprotection. Amlodipine, a light-sensitive drug, was formulated into a liquisolid tablet using Avicel (carrier) and silicone/titanium dioxide (coating material). This system showed improved photostability, retaining higher drug content after light exposure, outperforming conventional coating methods. [34]

Complexation

Complexing photosensitive drugs with agents like caffeine can enhance their photostability. For example, riboflavin's stability in aqueous solution improves when complexed with caffeine, particularly at pH 6. [22]

Cyclodextrins (CDs) can form inclusion complexes with various compounds through non-covalent interactions. This "host-guest" chemistry is a key research area, where CD nanocavities alter the photophysical and photochemical properties of encapsulated drugs, creating new opportunities for drug stabilization and delivery. [35]

Complexing drugs with cyclodextrins (CDs) can enhance photostability. Examples include:

- Doxycycline hyclate and phenylpropanoids with β-cyclodextrin
- Naproxen with 2-hydroxypropyl-β-CD
- Nifedipine with β-CD, HP-β-CD, and DM-β-CD
- Loratadine with α- and γ-CDs
- Isradipine with methyl β-CD
- Barnidipine in CD-in-liposome matrices

- These complexes show improved stability against light-induced degradation. [36,37,4]

Solid dispersion

Solid dispersions can enhance both drug solubility and photostability. By using water-soluble polymers as carriers, solid dispersions create a protective environment that improves drug stability against light-induced degradation. In a solid dispersion of diflunisal with Eudragit RS 100, the polymer network reduced the drug's photosensitizing activity by affecting the electron-trapping reaction, a key step in photodegradation. [38]

Curcumin, a light-sensitive compound in turmeric, degrades under UV irradiation. However, dispersing it in polymer matrices like Eudragit E PO or Hydroxypropyl methylcellulose-acetate succinate (HPMC-AS) provides strong protection against UV-induced degradation, enhancing its photostability compared to its raw form. [39]

Addition of excipients

Antioxidants

Light-sensitive molecules can degrade when excited by photosensitizers and free radicals. To mitigate this, two effective strategies are:

1. Removing oxygen (e.g., purging with nitrogen)
2. Adding antioxidants

Antioxidants can be chosen based on their redox potential relative to the drug, helping to prevent light-induced degradation. [4]

Spectral overlay

Blocking or reducing unwanted radiation exposure is a direct way to protect light-sensitive drugs and substances. Spectral overlay involves adding a compound that absorbs light at similar wavelengths as the photosensitive drug, effectively shielding the drug from degradation. UV-absorbers are commonly used for this purpose. [40]

Colorants, Opacifiers, and Coating Agents

Adding colorants, opacifiers, or coating agents can enhance photostability by absorbing photons. Certain compounds like curcumin, riboflavin, and azorubin can provide light protection to photosensitive formulations, such as molsidomine tablets. To shield photosensitive drugs from light, tablet manufacturers often use opacifiers and coating agents.

Colorants like iron oxides (yellow, red, black) can serve as effective opacifiers, protecting drugs like sorivudine from degradation. The particle size of pigments affects their light absorption and scattering abilities. Even distribution of these pigments on drug particles enhances their protective effect, leading to better photostability. [41,42]

Photo stabilizing excipient	Inactive ingredient	Drug name
Antioxidant	Sodium thiosulfate Sodium sulfite Glycine Alpha tocopherol	Minioxidil Daunorubicin hydrochloride Furosemide Vitamin C
UV absorber	Eusolex 6300 Riboflavin Curcumin, riboflavin, azorubin	Diclofenac gel Molsidomine Molsidomine
Colourants/opacifiers	Erythrosine Titanium dioxide, tartrazine	Sorivudine Nifedipine

Table 4: List of Excipients Utilized to Enhance the Photostability of Photodegradable Drugs [4]

Packaging material

A common way to protect light-sensitive molecules is through proper packaging. Using amber-coloured glass or plastic containers effectively blocks UV light, shielding photolabile drugs from degradation. Light-sensitive medications, such as riboflavin, prednisolone, and nandrolone sulfate eye drops, are often stored in brown glass bottles to protect them from light degradation. Another effective packaging method is wrapping containers with aluminium foil, which blocks UV and visible light. This method has shown high photoprotective effects, as demonstrated with riboflavin solutions. Protecting proteins from light exposure is crucial to preserve their potency. Effective packaging, such as using containers and cardboard boxes, provides good photoprotection and prevents degradation. [43]

Montmorillonite Methods

Montmorillonite (Al2H2O12Si4), a type of clay mineral, has been investigated as an excipient to enhance the photostability of light-sensitive drugs. When combined with drugs like piroxicam, it forms hybrids that show improved protection against light degradation. [44]

CONCLUSION

Light-stability testing of pharmaceuticals helps determine how products will hold up in real-world use and storage. When exposed to light, photosensitive drugs can undergo chemical changes, potentially losing effectiveness or even causing adverse effects due to the formation of reactive products. This review highlights past studies on light-induced degradation of pharmaceutical ingredients, providing valuable insights for developing photostable products. Knowing how pharmaceutical products break down when exposed to light is key to taking the right steps to protect them and ensure their stability during manufacturing.

REFERENCE

1. Vukićević M. Formulation of photoreactive drug substances: The role of excipients and type of preparation.
2. Aulton ME. Pharmaceutics: The science of dosage form design. (No Title). 2002 Dec 5.
3. Ahmad I, Ahmed S, Anwar Z, Sheraz MA, Sikorski M. Photostability and photo stabilization of drugs and drug products. International Journal of Photoenergy. 2016;2016(1):8135608.
4. Janga KY, King T, Ji N, Sarabu S, Shadambikar G, Sawant S, Xu P, Repka MA, Murthy SN. Photostability issues in pharmaceutical dosage forms and photo stabilization. Aaps Pharmscitech. 2018 Jan;19:48-59.
5. Bhalekar MR, Harinarayana D, Madgulkar AR, Pandya SJ, Jain DK. Improvement of photostability in formulation: A review. Asian Journal of Chemistry. 2008 Oct 1;20(7):5095.
6. Glass BD, Novák C, Brown ME. The thermal and photostability of solid pharmaceuticals. Journal of thermal analysis and calorimetry. 2004 Sep;77:1013-36.
7. Tønnesen HH. Formulation and stability testing of photolabile drugs. International Journal of pharmaceutics. 2001 Aug 28;225(1-2):1-4.
8. Ferguson J. Fluoroquinolone photosensitization: a review of clinical and laboratory studies. Photochemistry and photobiology. 1995 Dec;62(6):954-8.
9. Hayashi N, Nakata Y, Yazaki A. New findings on the structure-phototoxicity relationship and photostability of fluoroquinolones with various substituents at position 1. Antimicrobial agents and chemotherapy. 2004 Mar;48(3):799-803.
10. Guideline IH. Stability testing: photostability testing of new drug substances and products Q1B. Geneva: ICH. 1996 Nov;172.
11. Allain L, Baertschi SW, Clapham D, Foti C, Lantaff WM, Reed RA, Templeton AC, Tønnesen HH. Implications of in-use photostability: Proposed guidance for photostability testing and labeling to support the administration of photosensitive pharmaceutical products, part 3. Oral drug products. Journal of pharmaceutical sciences. 2016 May 1;105(5):1586-94.
12. Baertschi SW, Alsante KM, Tønnesen HH. A critical assessment of the ICH guideline on photostability testing of new drug substances and products (Q1B): recommendation for revision. Journal of pharmaceutical sciences. 2010 Jul;99(7):2934-40.
13. Thoma K, Klimek R. Photostabilization of drugs in dosage forms without protection from packaging materials. International journal of pharmaceutics. 1991 Jan 15;67(2):169-75.
14. Chen C, Zhao Q, Feng L, Zhang LQ. Photodegradation performance and mechanisms of carbamazepine and its impact factors. Huan jing ke xue= Huanjing kexue. 2012 Dec 1;33(12):4340-5.
15. Lachman L, Lieberman HA, Kanig JL. The theory and practice of industrial pharmacy. Philadelphia: Lea & Febiger; 1976.
16. Shende MA, Marathe RP. REVIEW ON PHOTOSTABILITY STUDIES OF FORMULATION.

17. Xuexiang H, Yong C, Yulun N, Chun H. Photodegradation of tetracyclines compound in aqueous solution under different light irradiation. Chinese Journal of Environmental Engineering. 2012;6(8):2465-9.
18. ZHU XD, WANG YJ, SUN RJ, ZHOU DM. Effect of solution pH on photodegradation and photocatalytic degradation of tetracyclines. Journal of Ecology and Rural Environment. 2012 Nov 25;28(6):742-5.
19. Albini A, Fasani E, editors. Drugs, photochemistry and photostability.
20. Zafiriou OC, True MB. Nitrite photolysis in seawater by sunlight. Marine Chemistry. 1979 Aug 1;8(1):9-32.
21. Devleeschouwer V, Roelandts R, Garmyn M, Goossens A. Allergic and photoallergic contact dermatitis from ketoprofen: results of (photo) patch testing and follow-up of 42 patients. Contact Dermatitis. 2008 Mar;58(3):159-66.
22. Ahmad I, Sheraz MA, Ahmed S, Shaikh RH, Vaid FH, ur Rehman Khattak S, Ansari SA. Photostability and interaction of ascorbic acid in cream formulations. Aaps Pharmscitech. 2011 Sep;12(3):917-23.
23. Klelemen H, Hancu G, Kacsó E, Papp LA. Photosensitivity reactions induced by photochemical degradation of drugs. Advanced Pharmaceutical Bulletin. 2021 May 29;12(1):77.
24. Gröllmann U, Schnabel W. Free radical-induced oxidative degradation of polyacrylamide in aqueous solution. Polymer degradation and stability. 1982 May 1;4(3):203-12.
25. Yousif E, Haddad R. Photodegradation and photostabilization of polymers, especially polystyrene. SpringerPlus. 2013 Aug 23;2(1):398.
26. Budai M, Szabó Z, Zimmer A, Szögyi M, Gróf P. Studies on molecular interactions between nalidixic acid and liposomes. International journal of pharmaceutics. 2004 Jul 26;279(1-2):67-79.
27. Manconi M, Valenti D, Sinico C, Lai F, Loy G, Fadda AM. Niosomes as carriers for tretinoin: II. Influence of vesicular incorporation on tretinoin photostability. International Journal of Pharmaceutics. 2003 Jul 24;260(2):261-72.
28. Habib MJ, Asker AF. Photostabilization of riboflavin by incorporation into liposomes. PDA Journal of Pharmaceutical Science and Technology. 1991 May 1;45(3):124-7.
29. Bandak S, Ramu A, Barenholz Y, Gabizon A. Reduced UV-induced degradation of doxorubicin encapsulated in polyethyleneglycol-coated liposomes. Pharmaceutical research. 1999 Jun;16(6):841-6.
30. Lucks S, Muller R, inventors; Medac Gesellschaft fuer Klinische Spezialpraeparate mbH, assignee. Medication vehicles made of solid lipid particles (solid lipid nanospheres-SLN). 25615/92A. 1996 Sep 26.
31. Carlotti ME, Sapino S, Peira E, Gallarate M, Ugazio E. On the photodegradation of dithranol in different topical formulations: use of SLN to increase the stability of the drug. Journal of Dispersion Science and Technology. 2009 Nov 4;30(10):1517-24.
32. Demchak RJ, Dybas RA. Photostability of abamectin/zein microspheres. Journal of Agricultural and Food Chemistry. 1997 Jan 20;45(1):260-2.
33. Pecora TM, Cianciolo S, Catalfo A, De Guidi G, Ruozi B, Cristiano MC, Paolino D, Graziano AC, Fresta M, Pignatello R. Preparation, characterization and photostability

assessment of curcumin microencapsulated within methacrylic copolymers. Journal of Drug Delivery Science and Technology. 2016 Jun 1;33:88-97.
34. Khames A. Liquisolid technique: a promising alternative to conventional coating for improvement of drug photostability in solid dosage forms. Expert opinion on drug delivery. 2013 Oct 1;10(10):1335-43.
35. El-Kemary M, Douhal A. Photochemistry and photophysics of cyclodextrin caged drugs: Relevance to their stability and efficiency. InCyclodextrin materials photochemistry, photophysics and photobiology 2006 Jan 1 (pp. 79-105). Elsevier.
36. Rivas-Granizo PE, Giorgetti L, Ferraz HG. Photostability of loratadine inclusion complexes with natural cyclodextrins. International Journal of Photoenergy. 2015;2015(1):583052.
37. Mielcarek J, Daczkowska E. Photodegradation of inclusion complexes of isradipine with methyl-β-cyclodextrin. Journal of pharmaceutical and biomedical analysis. 1999 Nov 1;21(2):393-8.
38. Pignatello R, Ferro M, De Guidi G, Salemi G, Vandelli MA, Guccione S, Geppi M, Forte C, Puglisi G. Preparation, characterisation and photosensitivity studies of solid dispersions of diflunisal and Eudragit RS100® and RL100®. International journal of pharmaceutics. 2001 May 7;218(1-2):27-42.
39. Li J, Lee IW, Shin GH, Chen X, Park HJ. Curcumin-Eudragit® E PO solid dispersion: a simple and potent method to solve the problems of curcumin. European Journal of Pharmaceutics and Biopharmaceutics. 2015 Aug 1;94:322-32.
40. Thoma K, Spilgies H. Photostabilization of solid and semisolid dosage forms. InPharmaceutical photostability and stabilization technology 2006 Sep 18 (pp. 347-368). CRC Press.
41. Piechocki JT, Thoma K, editors. Pharmaceutical photostability and stabilization technology. CRC Press; 2006 Sep 18.
42. Desai DS, Abdelnasser MA, Rubitski BA, Varia SA. Photostabilization of uncoated tablets of sorivudine and nifedipine by incorporation of synthetic iron oxides. International journal of pharmaceutics. 1994 Feb 25;103(1):69-76.
43. Kerwin BA, Remmele Jr RL. Protect from light: photodegradation and protein biologics. Journal of pharmaceutical sciences. 2007 Jun 1;96(6):1468-79.
44. Ambrogi V, Latterini L, Nocchetti M, Pagano C, Ricci M. Montmorillonite as an agent for drug photostability. Journal of Materials Chemistry. 2012;22(42):22743-9.