

Thermal Stability of Various APIs

Note that stability to elevated temperature can be contingent on other factors including other excipients, solvents, preservatives found in the preparation or chemical characteristics such as pH of the solution. The below is meant to provide information on potential temperature tolerances of various APIs. Stability testing is recommended on specific preparations or combinations to verify the suitability of the sterilization method.

Active Pharmaceutical Ingredient	Autoclave*	Dry Heat**	General Information on Thermal Stability
Acetylcysteine ¹	No	No	Studies on thermal degradation of acetylcysteine have found significant degradation of stock solutions at 80°C over 3 hours.
Alprostadiol ²	No	No	Alprostadiol is significantly susceptible to thermal degradation
Amikacin Sulfate ^{3,4}	Yes	Unknown	Information exists to suggest amikacin aqueous solutions are acceptable for autoclave sterilization. With regards to dry heat sterilization, information was unavailable. One study noted a small amount of degradation with amikacin dry powder exposed to 70°C over 48 hours, but no studies were available at higher temperatures consistent with dry heat sterilization
Amphotericin B ^{5,6}	No	No	Though some information suggests limited amphotericin B stability, and even potentially enhanced activity at temperatures up to 41°C in some trials, amphotericin B is not known to be stable to temperatures consistent with autoclave or dry heat sterilization.
Anastrozole ^{30,31}	Yes	Unknown	One study on bulk drug powder and anastrozole tablets found minimal degradation after exposure to 105°C for 6 hours, but higher temperatures were not evaluated. Another study of anastrozole and testosterone subcutaneous pellets stated the method of sterilization was autoclave at 121°C for 25 minutes at 20-25psi
Arginine HCl ^{7,8}	Yes	Unknown	Though information on dry heat sterilization of arginine HCl was unavailable, some information exists to support its stability to autoclave. Some studies have evaluated the effect of arginine at 75°C for the prevention of protein aggregation as well in some preparations.
Ascorbic Acid ⁹	No	No	Ascorbic acid has known thermal instability
Atropine Sulfate ^{7,10}	Yes	No	The presence of a degradant (aprotropine sulphate) as been noted after exposure to 150°C, so while some information supports autoclave stability, dry heat sterilization is not recommended
Biotin ¹¹	Unknown	No	Limited information is available regarding biotin thermal stability, some sources suggest good stability in solution in excess of 100°C, making this API potentially a candidate for autoclave
Bupivacaine HCl ^{12,13}	Yes	Unknown	Bupivacaine HCl solutions are stable to autoclave, information on dry heat sterilization was not available, but some studies on heat degradation suggest that there may be elevated thermal stability
Calcium Chloride ⁷	Yes	Unknown	Handbook on Pharmaceutical Manufacturing Formulations contains autoclave sterilized formulations, suggesting stability to autoclave
Calcium Gluconate ^{7,15}	Yes	No	Calcium gluconate undergoes thermal degradation at temperatures greater than 150°C
Cholecalciferol	No	No	One study of vitamin D ₃ in oil at various temperatures found that samples treated at 100 °C for 30 min showed no significant reduction, while samples treated at 150 and 180 °C were significantly degraded
Cyanocobalamin ¹⁷⁻¹⁹	Yes	No	While the package insert for cyanocobalamin states that it may be sterilized via autoclave without significantly effecting potency, data on higher temperatures suggests that degradation may occur if dry heat sterilization is attempted
Cyclosporine ^{20,21}	Yes	Unknown	Some studies evaluation aqueous preparations of cyclosporine have noted stability to autoclave at 121°C for 15 minutes at 15 psi
Cysteine ^{22,23,59}	Unknown	Unknown	Information is limited, one study on degradation of dry powder amino acids found cysteine degradation starting at 200°C suggesting some potential thermal stability, other studies have corroborated similar temperatures. However, specific information regarding sterilization under steam heat was not found in the literature
Dexamethasone Sodium Phosphate ²⁴	No	No	The package insert for dexamethasone sodium phosphate recommends against autoclaving due to dexamethasone sodium phosphate thermal instability

Dexpanthenol ^{25,26}	Unknown	Unknown	Information regarding dexpanthenol thermal stability at temperatures needed for terminal sterilization was unavailable, one study found good thermal stability at 40°C for 6 hours, and another found no degradation in solution at 80°C over 5 hours, but higher temperatures were not evaluated
Edetate Disodium ²⁷	Yes	Unknown	Information suggests EDTA degradation at temperatures greater than 200°C
Estradiol ^{61,62}	No	No	One study of estradiol found nearly 10% degradation of bulk drug hormone and hormone in an aqueous cream formulation when exposed to 90°C for 24 hours, another found approximately 30% degradation after exposure to 180°C for 30min
Estradiol Valerate	Unknown	Unknown	Insufficient information to determine thermal stability
Finasteride ⁵⁵	No	No	While finasteride does have some thermal stability, greater than 10% degradation has been noted with exposure to 60-70°C for 90 minutes
Folic Acid ^{28,29}	Yes	No	While some data exists to support stability to autoclave, some data on dry heat suggests degradation at temperatures consistent with those for dry heat sterilization
Glutathione ³²	No	No	Little information is available on glutathione stability in solution under heat, but some data from food studies suggests complete degradation at temperatures of 75°C or above.
Hydroxocobalamin ³³	No	No	Thermal studies have noted degradation at temperatures below those required for autoclave sterilization
Lidocaine	Unknown	Yes	One study found lidocaine degradation to occur beginning at approximately 196°C. Note that though lidocaine has a high temperature for degradation, its melting point is below the temperature typically used for dry heat sterilization. Studies on the base form of lidocaine regarding stability to steam heat were unavailable.
Lidocaine HCl ³⁴	Yes	Unknown	The package insert for lidocaine HCl Injection specifies that the product may be autoclaved at 121°C for 15min at 15psi. Studies on lidocaine exposure to dry heat have shown stability at least to 120°C for 72 hours
Lysine ³⁴	No	No	One study on lysine at water activity 0.3, 0.5, and 0.7 found significant degradation when exposed to temperatures in excess of 75°C
Magnesium Chloride ^{7,36}	Yes	Yes	Thermal degradation studies on magnesium chloride note hydrolysis starting at 203°C, higher than typical for dry heat sterilization
Magnesium Sulfate ^{37,38}	Yes	Yes	Decomposition studies on magnesium sulfate suggest temperatures much higher than those used for dry heat sterilization are needed to degrade magnesium sulfate
Methionine ³⁹	Unknown	Unknown	One study noted methionine stability to autoclave, another noted degradation between 190-240°C
Methylcobalamin ³³	No	No	Thermal degradation studies between 100-121°C have noted significant methylcobalamin degradation
Minoxidil ⁵⁵	No	No	While minoxidil does have some thermal stability, some limited degradation has been noted with exposure to 60-70°C for 90 minutes, suggesting thermal degradation does occur
Nandrolone Decanoate ⁶³	Unknown	Unknown	Though some degradation studies on other nandrolone salts, such as nandrolone propionate, demonstrated stability at 150°C and degradation at higher temperatures of 200°C, specific information on nandrolone decanoate in oil was unavailable
Niacinamide ^{7,41}	Unknown	No	Some B-complex formulations containing thiamine, riboflavin-r-phosphate, pyridoxine HCl, and niacinamide have procedures requiring autoclave sterilization at 121°C for 20 minutes per the Handbook on Pharmaceutical Manufacturing Formulations, suggesting stability to autoclave. Niacinamide has a melting point beginning at 129°C
Papaverine HCl ⁷	Unknown	No	Insufficient information available to determine if autoclave sterilization is appropriate. One formula from the Handbook on Injectable Drugs sterilized a papaverine containing formula at 121°C for 30 minutes
Phentolamine Mesylate	Unknown	Unknown	Insufficient information to determine thermal stability
Progesterone ^{7,51,52}	Unknown	Possible	One study evaluating progesterone at 60°C over one week didn't note degradation. Another study of progesterone in pharmaceutical waste noted that temperatures of 300°C for 15 minutes were needed to degrade progesterone completely (temperatures between 200-350°C were evaluated).
Pyridoxine HCl ^{7,41}	Yes	No	Information suggests that pyridoxine HCl is stable at temperatures required for autoclave, tests at 121°C for 15 minutes have not noted pyridoxine degradation
Riboflavin-5-Phosphate ⁷	Unknown	No	Some B-complex formulations containing thiamine, riboflavin-r-phosphate, pyridoxine HCl, and niacinamide have procedures requiring autoclave sterilization at 121°C for 20 minutes per the Handbook on Pharmaceutical Manufacturing Formulations, suggesting stability to autoclave.
Semaglutide ⁴²	Unknown	Unknown	One study exposed semaglutide solutions to 105°C for 15 hours and noted less than 3% degradation

Sodium Bicarbonate⁴⁴	No	No	Some studies note that exposure of sodium bicarbonate to heat and moisture can result in the formation of carbon dioxide, water, and sodium carbonate
Tacrolimus^{53,54}	No	No	One study evaluating stability of tacrolimus aqueous solution noted minimal degradation after exposure to 60°C for 24 hours suggesting some thermal stability, however, one study analyzing stability to autoclave of several aqueous tacrolimus preparations noted significant degradation.
Testosterone^{30,46,47,48}	Yes	Unknown	Testosterone: One study of anastrozole and testosterone subcutaneous pellets stated the method of sterilization was autoclave at 121°C for 25 minutes at 20-25psi for the combination and 40 minutes, all other parameters being the same, for testosterone pellets alone. One study of testosterone exposed to 100°C for 4 hours though did not note significant degradation Testosterone Cypionate: one study observed no degradation when testosterone was exposed to 80°C for 48 hours Testosterone Undecanoate: one study on testosterone undecanoate capsules exposed to 105°C over 48 hours found over 18% degradation.
Tetracaine HCl⁵⁸	Yes	Unknown	The tetracaine HCl injection package insert states that the vial may be autoclaved at 121°C at 15psi for 15 minutes
Thiamine HCl^{7,45}	Unknown	No	Some B-complex formulations containing thiamine, riboflavin-r-phosphate, pyridoxine HCl, and niacinamide have procedures requiring autoclave sterilization at 121°C for 20 minutes per the Handbook on Pharmaceutical Manufacturing Formulations, suggesting stability to autoclave. Information suggests that thiamine heat stability is temperature related, with solutions at pH 3 being much more stable than those at pH 6 in one study.
Tirzepatide⁶⁰	Unknown	Unknown	One study noted just over 3% degradation with dry heat exposure to 70°C over 24 hours
Tocopherol Acetate (Vitamin E Acetate)⁴⁹	Unknown	Unknown	One study of vitamin E in a cream found thermal stability up to 250°C at which point there was a significant degradation curve
Vancomycin HCl⁵⁰	No	No	One study noted vancomycin HCl degradation after exposure to 80°C for 300 minutes.
Zinc^{56,57}	Yes	Yes	Zinc Sulfate – the Zinc Sulfate Compounded Injection USP Monograph notes autoclave as the method for sterilization. One study notes zinc sulfate stability up to 680°C Zinc Chloride – Information not available on autoclave, but one study found zinc chloride to be stable up to temperatures of 320°C Zinc Acetate – information not available

*Autoclave refers to steam heat conditions of 121°C or greater under pressure, typically about 15psi

**Dry heat refers to non-aqueous heat exposure typically above 160°C

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