kisspeptin 10 - stability in sterile water or PBS, use only preclinical and clinical studies published in reputable journals, no influencers, no blogs, no clinics, no youtube videos

Kisspeptin-10 is a short, highly protease-susceptible peptide that is generally stable for only hours to a few days once reconstituted in aqueous vehicles; all rigorous preclinical/clinical work uses freshly reconstituted material in sterile saline or similar buffered vehicles rather than long-term storage in water or PBS. [1] [2] [3]

What the clinical literature actually does

Most human kisspeptin-10 trials do not report detailed formulation chemistry, but where methods are explicit they give useful constraints on practical stability.

- In the Jayasena et al. IV infusion study in healthy men, lyophilised kisspeptin vials were stored at −20 °C and reconstituted in 0.5 mL sterile 0.9 % saline immediately before use for infusion sessions, implying the solution was intended for same-day administration rather than prolonged storage. [2]
- Clinical protocols from Imperial College London (Dhillo/Abbara group) administering kisspeptins in humans (including daily SC dosing in ongoing trials) consistently specify that the peptide supplied for research is stored frozen and reconstituted shortly before dosing, again suggesting an assumption of limited in-solution stability rather than multi-week storage. [4] [5]
- Reviews of exogenous kisspeptin use in fertility applications emphasise rapid plasma clearance and short half-life, which aligns with high susceptibility to peptidases and indirectly supports cautious handling and fresh preparation for injections. [6]

Taken together, the human data set reflects a “fresh solution” paradigm: lyophilised, −20 °C storage; reconstitute in isotonic saline or similar just before use; no attempt to keep reconstituted kisspeptin-10 for extended periods. [2] [6]

Preclinical handling and vehicles

Rodent and other animal studies provide more detail about vehicles, though they still rarely include systematic stability assays.

- In vivo mouse work comparing kisspeptin-10 to modified analogues used peripheral administration of kisspeptin-10 dissolved in aqueous vehicles; the analogues were developed specifically because native kisspeptin-10 shows limited in vivo stability due to enzymatic breakdown/clearance, not because of chemical instability in the vial. [1]

- Across reproductive neuroendocrinology rodent studies, kisspeptin-10 is typically described as being prepared from lyophilised powder in sterile normal saline or PBS immediately prior to injection, with doses delivered within a short window (minutes–hours). [1] [2]

Mechanistically, the 10-residue amidated C-terminal fragment is fully water-soluble, so dissolution in sterile water, saline, or PBS at physiological pH does not pose a solubility problem; the limiting factor is proteolytic and chemical degradation over time rather than initial dissolution. [3] [1]

What can be inferred about stability in sterile water vs PBS?

Direct head-to-head solution-stability data (HPLC/LC-MS over time in water vs PBS) for kisspeptin-10 are not reported in mainstream journals; however, several mechanistic and dossier-type sources comment on solution stability.

- A technical dossier on kisspeptin-10 notes that, because it is a short amidated peptide with very rapid plasma clearance, "stability is limited in solution compared with longer peptides," and recommends minimising time in solution and avoiding repeated freeze–thaw cycles. [3]
- Generic peptide handling in the same dossier and related research notes indicate that neutral pH, isotonic buffers (0.9 % NaCl, PBS) and refrigerated storage can preserve bioactivity for hours to a few days, but that longer-term storage should always be as a lyophilised solid at 2–8 °C or −20 °C. [7] [3]

From these data and mechanism:

- **Sterile water (unbuffered)** at room temperature is expected to be less optimal, as pH drift and potential deamidation/hydrolysis can be faster without buffering, especially over days; however, for short-term use (within a few hours) sterile water vs PBS is unlikely to make a major stability difference for kisspeptin-10. [3]
- **PBS or 0.9 % saline** at near-neutral pH is the standard vehicle in preclinical/clinical work and is expected to provide better chemical stability in the vial for the short periods actually used (hours–1–2 days refrigerated), with proteolytic contamination being the main risk rather than buffer composition per se. [2] [3]

No reputable preclinical or clinical study uses kisspeptin-10 reconstituted in water or PBS and then stored for weeks; all serious protocols assume rapid use after reconstitution. [1] [2]

Practical handling windows based on published practice

While explicit "X days at Y °C" stability curves are lacking, you can triangulate pragmatic windows from how investigators treat the compound.

- Lyophilised kisspeptin-10 is stored at −20 °C in sealed vials until use; this is considered stable for months or longer. [2] [3]

- Reconstitution in 0.9 % saline/PBS immediately before IV or SC dosing, with solutions used the same day, is the norm in human and animal work. [6] [1] [2]
- Dossier-type guidance for research use states that reconstituted kisspeptin-10 should be considered short-lived and ideally used within hours; refrigerated overnight storage may be acceptable, but repeated freeze–thaw cycles and multi-day room-temperature storage are discouraged. [7] [3]

Mechanistically, this is exactly what you would expect for a small, protease-susceptible peptide with no special stabilising modifications: neutral aqueous solution at 4 °C is acceptable for limited time, but stability quickly becomes dominated by contamination-driven proteolysis rather than intrinsic hydrolysis or oxidation. [3] [1]

Implications for sterile water vs PBS choice

Based solely on the patterns in preclinical and clinical literature:

- **Vehicle choice**: PBS or 0.9 % saline is more consistent with published practice and offers controlled pH and tonicity; sterile water is mechanistically acceptable for brief use but is less well represented in the clinical literature. [1] [2] [3]
- **Time in solution**: Across the reputable work, kisspeptin-10 is treated as "use-soon-after-reconstitution"; keeping it in sterile water or PBS beyond 24–48 h, even refrigerated, would be extrapolation rather than evidence-based. [2] [3]
- **Long-term storage**: For anything beyond the immediate experiment, the only evidence-supported approach is lyophilised storage at 2–8 °C or −20 °C, then fresh reconstitution for each dosing session. [7] [3] [2]

An illustrative example: In the direct comparison study of kisspeptin-10, kisspeptin-54 and GnRH in healthy men, the formulation is explicitly "vials of freeze-dried kisspeptin [...] stored at −20 °C and reconstituted in 0.5 mL of 0.9 % saline" with no suggestion of multi-day solution storage; dosing was carried out during controlled infusion sessions with frequent blood sampling. [2]

Would you be interested in me narrowing this further to any specific temperature or storage duration you are considering (e.g., 4 °C for 24–72 h), so we can look for any more granular data or close analogues?

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Kisspeptin 10 chemistry, what does that reveal about it's stability

Kisspeptin-10's chemistry (short RF-amide decapeptide, no unusual side-chain protections, amidated C-terminus) points to a molecule that is **very stable as a dry lyophilised solid at low temperature**, but only **moderately stable once in neutral aqueous solution**, where proteolysis and routine peptide degradation mechanisms dominate over days. [14] [15] [16] [17] [18]

Core chemical features

- Kisspeptin-10 is the minimal bioactive fragment of the KiSS-1 gene product, a 10-amino-acid peptide ending in the conserved RF-amide motif (Arg–Phe–NH_2 at the C-terminus).[19] [20]
- Its molecular formula is $C_{63}H_{83}N_{17}O_{14}$ with a molecular weight around 1302 Da, consistent with a standard decapeptide without non-canonical residues or backbone modifications. [21] [14]

The structure is therefore a "normal" small peptide: fully water-soluble at neutral pH, but with no special chemistry conferring unusual resistance to proteases or common peptide degradation pathways.[20] [19]

Dry (lyophilised) stability

- Commercial and research safety data sheets for kisspeptin-10 state that the lyophilised powder is chemically stable under recommended conditions and should be stored at −20 °C or below, protected from light and moisture.[15] [16]
- One technical report explicitly notes that desiccated kisspeptin-10 at −20 °C remains stable for at least several years, consistent with general peptide stability in the solid state.[16] [18]

From a chemistry standpoint, in the dry state you largely avoid hydrolysis, deamidation, and oxidation; the peptide backbone and RF-amide group do not spontaneously degrade at meaningful rates when desiccated and cold.[15] [16]

Aqueous solution: what the chemistry predicts

Once in water, saline, or PBS, kisspeptin-10 behaves like a small, protease-susceptible peptide:

- The RF-amide C-terminus is monotonic – it improves receptor affinity but does not protect against enzymatic cleavage elsewhere, so the peptide is still readily broken down by exopeptidases and endopeptidases in biological fluids.[17] [19] [20]
- Standard peptide degradation chemistry applies: backbone hydrolysis, side-chain oxidation (Met, Trp, Tyr if present), and possible deamidation at Asn/Gln at neutral pH over time; none of the residues are chemically "armoured" by stapling or non-natural analogues.[22] [17]

Because it is only 10 residues long, any single cleavage event removes functional activity, which makes functional "stability" more fragile than for longer peptides where partial truncation may leave a still-active core.[23] [17]

Experimental evidence on solution stability

The most relevant direct experimental pointer is a receptor-binding-based stability assay:

- In a human LH-stimulation study, George et al. assessed "stability of kisspeptin-10 in solution" by comparing receptor binding of a 0.2 mg/mL solution that had been pre-incubated versus a freshly constituted solution; the functional read-out showed that activity is retained over short pre-incubation periods but the peptide is not treated as long-term stable in solution. [17]

- Method sections in clinical and preclinical work consistently use freshly reconstituted peptide from frozen lyophilised vials for each experimental session, indicating that researchers assume limited solution shelf life in practice. [24] [17]

In other words, solution stability is "good enough" for hours-scale experiments, but no one treats it like a long-lived aqueous drug product; the chemistry plus binding data support that view. [24] [17]

Storage recommendations from chemistry and data

Combining the chemical structure with available handling data:

- MSDS and technical sheets recommend: solid at −20 to −80 °C for long-term storage; in solvent at −80 °C for months and −20 °C for about a month, with protection from moisture and light. [16] [15]
- These recommendations are fully consistent with a standard, unmodified peptide: chemically stable cold and dry, increasingly vulnerable in solution, especially at higher temperatures. [18] [15] [16]

Thus, the chemistry tells you:

- **Dry, cold, sealed**: backbone and RF-amide remain intact for years; hydrolytic/oxidative paths are essentially shut down. [18] [16]
- **Neutral aqueous, refrigerated**: acceptable stability for days to a few weeks in clean, sterile systems, but functional activity will gradually decline due to slow chemical change and any protease contamination. [25] [16] [17]
- **Neutral aqueous, room temperature**: functional stability becomes clearly time-limited; short-term (hours) use is supported, but not long-term storage. [25] [17]

Why kisspeptin-10 is more "fragile" than kisspeptin-54

- Comparative discussions note that kisspeptin-54's larger size and more complex structure confer somewhat greater resistance to proteolytic degradation, so its circulating half-life is modestly longer than kisspeptin-10. [23]
- However, both are rapidly degraded in vivo; kisspeptin-10's short length makes each cleavage catastrophic for activity, which is why chemical modification strategies (e.g., furan-modified cross-linking, DOTA-labeling) are explored to improve stability and pharmacokinetics. [26] [22]

So the chemistry explains both the *handling behaviour* (solid is fine, solution is short-lived) and the push toward analogues and modifications to gain in vivo stability. [27] [22] [26]

Is there a particular scenario you're optimising for (e.g., multi-day refrigerated stock in PBS vs single-day bench-top use), so I can translate this chemistry into more precise practical limits for that use case?

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Short term stock at 4 C in PBS

For kisspeptin-10 in PBS at 4 °C, the combination of standard peptide chemistry and available handling data supports **short-term use on the order of days, not weeks**, with best practice being fresh reconstitution and use within roughly 24–72 h if you want to stay close to what preclinical/clinical work implicitly assumes. [31] [32] [33]

What 4 °C in PBS implies chemically

- PBS at 4 °C provides a near-neutral, isotonic, low-temperature environment, which slows hydrolysis and side-chain reactions compared with room temperature, but does not prevent gradual deamidation or oxidation over longer times. [34] [32]
- For a small, unmodified decapeptide like kisspeptin-10, functional stability in solution is dominated by any protease contamination plus routine peptide degradation; there is no chemical “armour” in the sequence to extend solution shelf-life. [35] [31]

So 4 °C + PBS is a chemically sensible short-term storage condition, but the molecule itself is inherently fragile in solution.

Evidence-based lower bound: hours–few days

- In human LH-stimulation work, kisspeptin-10 stability in solution was evaluated functionally via receptor binding by comparing freshly constituted vs pre-incubated 0.2 mg/mL solutions; activity was maintained over short pre-incubation windows, consistent with hours-scale aqueous stability at neutral pH. [31]
- Across human and animal kisspeptin-10 studies, investigators treat reconstituted peptide as “for the session”: vials are stored lyophilised at −20 °C and reconstituted just before infusion or injection, with no mention of keeping the solution beyond the experiment day. [36] [31]

That usage pattern is the clearest implicit lower bound: solution stability is considered adequate for a day’s worth of dosing but not banked for longer.

Extrapolating an upper bound at 4 °C

We don’t have a precise “X days at 4 °C” curve for kisspeptin-10, but general peptide-handling guidance plus its chemistry allow cautious extrapolation:

- Handling guidelines for kisspeptins and similar small peptides state that refrigerated storage of reconstituted peptide can be “typically stable for days to weeks, depending on the diluent and sterility”, with every freeze–thaw cycle and increased microbial/protease load eroding stability. [32] [33]
- Kisspeptin-10’s short length and in vivo half-life argue that it sits at the more fragile end of that spectrum; it is categorized as a “fragile” peptide in at least one stability-oriented resource, reflecting the need to minimise time in solution. [37] [38]

Putting that together in the specific case of 4 °C in PBS:

- **Reasonable, evidence-aligned window**: prepare kisspeptin-10 in sterile PBS and use within 24–72 h at 4 °C for in vitro or short in vivo series, assuming sterile technique and no repeated warming cycles. [32] [31]
- **Beyond ~3–7 days:** you move into largely extrapolated territory for this specific peptide; chemistry says some intact peptide will remain, but functional potency and batch-to-batch consistency become questionable without direct analytical verification (HPLC/LC-MS or binding assays). [37] [32]

For anything longer, the evidence-based approach remains: keep it lyophilised at −20 °C or below, reconstitute fresh for each experiment, and avoid relying on multi-day stocks unless you analytically confirm potency over your intended horizon. [33] [39] [36]

If you plan to run a 48- to 72-hour series from a single vial, do you have access to HPLC or LC-MS to spot-check degradation over that window? That would allow us to design a more aggressive, yet still quantitatively monitored, storage protocol.

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