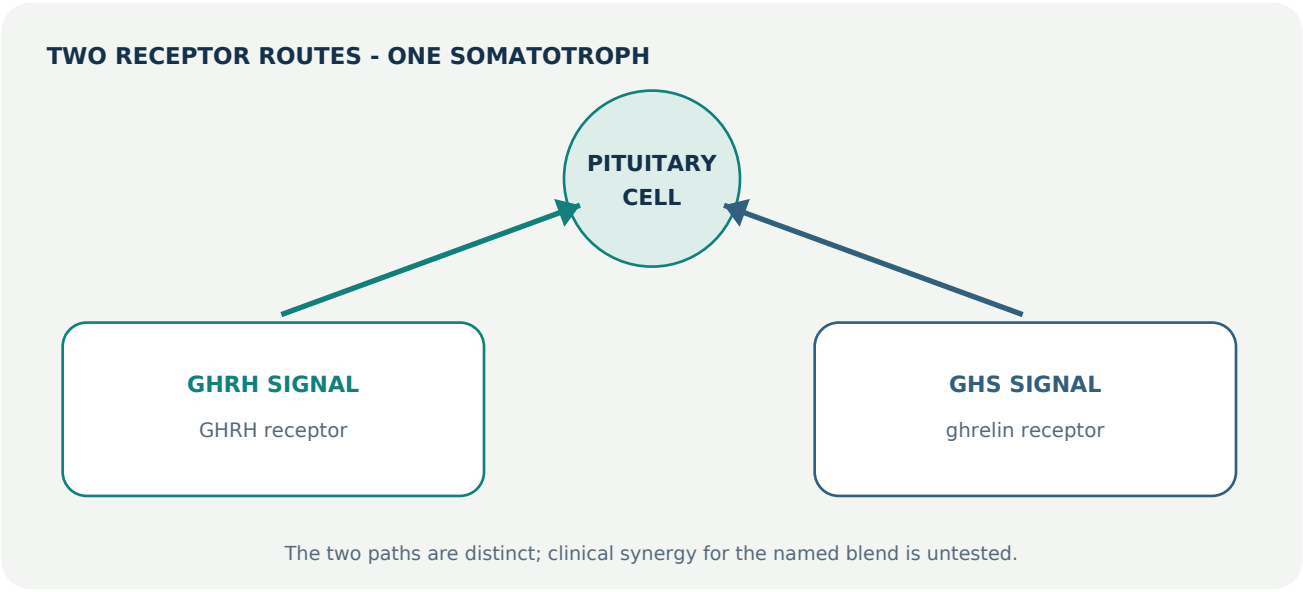
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Two Signals, One Question

CJC-1295 No DAC + Ipamorelin

The compelling biology of two growth-hormone secretagogue pathways - and the surprising gap between a persuasive mechanism and proof for a particular combination.



The two paths are distinct; clinical synergy for the named blend is untested.

A narrative scientific literature review | receptor biology, original human hormone studies, animal experiments, the difference between CJC-1295 with and without DAC, and what has not yet been tested.

Prepared by Vanguard Compound Research. Literature search and synthesis through 26 October 2026. This independently drafted educational review is not peer reviewed and does not evaluate or validate any commercial formulation, lot or supplier. No administration, dosing, reconstitution or self-experimentation instructions are provided. This publication has not been reviewed or approved by Health Canada.

BEFORE THE FIRST STUDY

Why two signals attracted so much attention

The pituitary gland is only about the size of a pea, yet its chemical messages influence growth, energy use and the repair and turnover of tissues. Growth hormone (GH) is one of those messages. It is not released as a steady stream. Instead, the body sends bursts shaped by sleep, nutrition, age, somatostatin and input from the hypothalamus. [1-3]

For decades, researchers have tried to understand whether that system can be stimulated through signals upstream of GH itself. One route is growth hormone-releasing hormone (GHRH), which binds the GHRH receptor on pituitary somatotrophs. Another is the growth-hormone secretagogue receptor, now recognized as the ghrelin receptor. Synthetic peptides can engage these routes in different ways. [1-4]

The attraction is immediate: if one signal opens a receptor pathway and a second amplifies it, might the endocrine response be greater than either signal alone? A classic human experiment in 1990 offered a fascinating answer for GHRH and the older peptide GHRP-6. The combined response was more than an uncomplicated sum of the individual responses. But that experiment was not performed with today's named CJC-1295 No DAC and Ipamorelin blend. [3]

> A strong biological reason to study a combination is **not** the same as clinical evidence that the combination improves sleep, body composition, recovery or health.
>
> EVIDENCE INTERPRETATION

The story becomes more interesting as the names are untangled. The most quoted human CJC-1295 trial investigated a molecule designed to bind blood albumin for prolonged exposure - the DAC-bearing form. By contrast, "CJC-1295 No DAC" is a marketplace label generally applied to a shorter modified GRF(1-29) peptide without that albumin-binding extension. Mixing those results together would give a misleading picture of the actual scientific record. [6-8]

Ipamorelin has a different evidence story: pharmacology in cultured cells and animals, a published human hormone-exposure study, and a controlled human trial in postoperative intestinal recovery that did not establish the hoped-for clinical benefit. Those findings are worth examining, but none establishes efficacy for a combined No DAC/Ipamorelin formulation. [4,5,9]

HOW THIS PAPER IS ORGANIZED

We begin with the receptor biology, then separate the DAC and No DAC identities, inspect individual human and animal studies, and finally consider what a properly designed future trial would need to show. Study citations correspond to directly linked primary publications or regulator documents in the reference library.

CHAPTER 01 / THE EVIDENCE STORY

Two doors into the same endocrine cell

An elegant biological hypothesis grew out of work on distinct receptor systems.

In a healthy endocrine axis, hypothalamic GHRH activates its receptor on the somatotroph. This receptor couples to intracellular cyclic AMP signaling. Ghrelin and synthetic growth-hormone secretagogues approach through a different receptor, GHSR1a, whose signaling uses calcium-linked and other downstream pathways. Both routes can affect GH release, but the whole-system outcome depends on the surrounding hormonal feedback loops. [1-4]

This is more than a semantic distinction between two peptides. Each ligand has its own affinity, receptor selectivity, distribution, metabolism and potential actions outside the pituitary. A compound that triggers a brief hormone peak need not resemble one that alters the pulse pattern over several days. The scientific question is therefore not simply whether both can raise GH; it is whether their particular timing, receptor engagement and feedback behavior can be characterized when combined. [3-8]

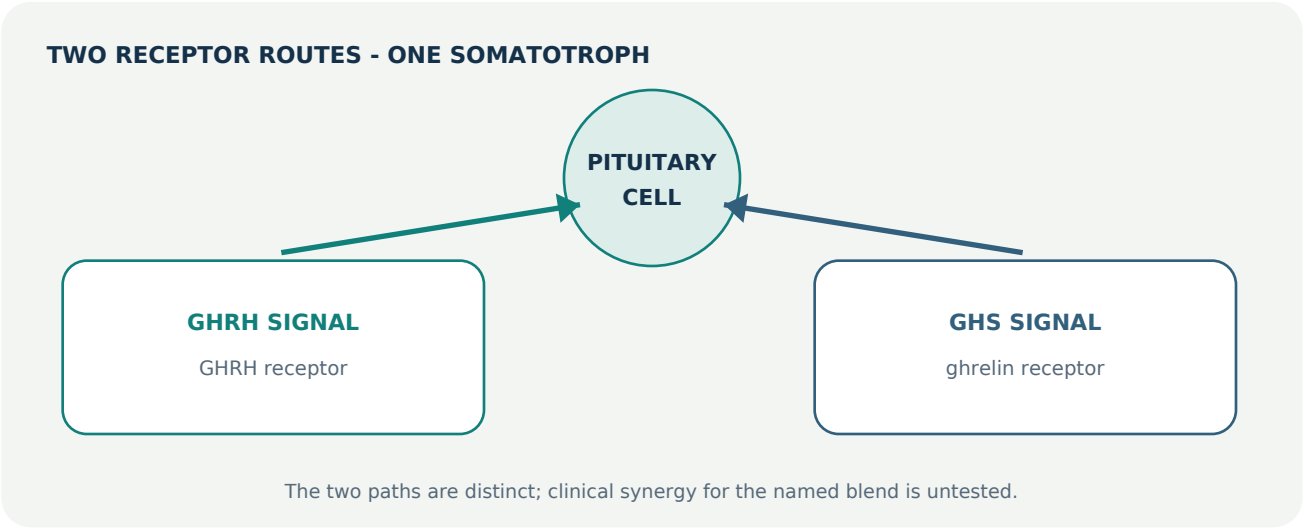


FIGURE 01. Conceptual receptor schematic. A GHRH-family signal and a ghrelin-receptor signal can influence the same endocrine system. It does not demonstrate efficacy of the named blend.

The 1990 experiment that launched the combination idea

Bowers and colleagues studied 18 normal men with the GHRH signal, the synthetic secretagogue GHRP-6, and the two together. Their central finding was acute GH-release synergy: the response to both stimuli exceeded what investigators would expect by a simple additive model. The experiment remains a foundational demonstration that GH regulation is multi-input rather than single-switch. [3]

But the identity of the test article matters. GHRP-6 is not ipamorelin. The GHRH used in that experiment was not the peptide now labeled CJC-1295 No DAC. Biological class membership allows a mechanistic hypothesis; it does not establish the size, duration or clinical consequences of an effect for new members of those classes. Even proof of synergistic GH secretion would be a biomarker result, not automatically a functional or therapeutic outcome.

KEY INTERPRETATION

The mechanistic precedent for dual-pathway stimulation is real and experimentally demonstrated in humans for older ligands. The exact combination named on this cover has a different, much thinner evidence base.

CHAPTER 02 / THE EVIDENCE STORY

The CJC-1295 naming trap

The most consequential word in the literature is the short suffix “DAC.”

In drug discovery, a few atoms can determine what an experiment actually means. Jetté and colleagues developed a modified 29-residue human GHRH fragment bearing substitutions and a terminal chemical extension designed to bind serum albumin. The long-lived conjugate became known as CJC-1295. In rats, the investigators detected its albumin-associated species in circulation, helping explain how its exposure differed from that of a conventional short GHRH fragment. [6]

In commercial research catalogs, however, "CJC-1295 No DAC" commonly designates modified GRF(1-29) without that albumin-binding chemical extension. This is a useful shorthand for identifying a research topic, but it is not proof of composition, analytical identity or equivalent human pharmacology. No-DAC terminology is not a substitute for a precise structural specification. [6]

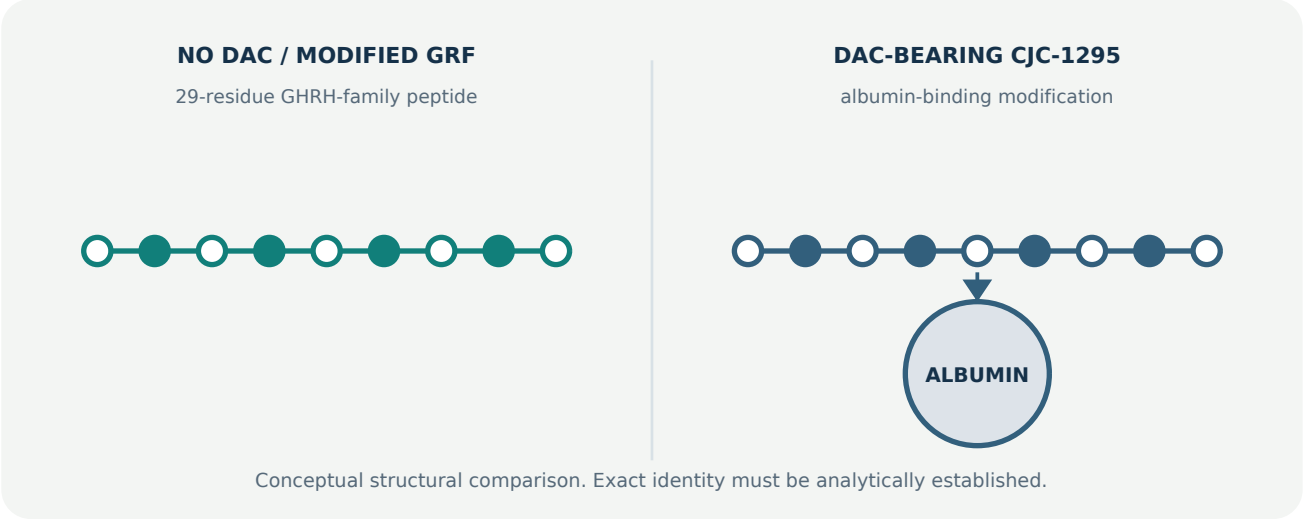


FIGURE 02. Conceptual distinction between a modified GRF fragment and the albumin-binding CJC-1295 construct. Not a structural formula and not a claim about any commercial vial.

What the famous 2006 study actually tested

Teichman and coauthors conducted two randomized, double-blind, placebo-controlled studies of the **long-acting DAC-containing CJC-1295** in healthy adults. They reported several-day elevations in circulating GH and IGF-I, with measured exposure persisting far beyond what is expected from a typical short GHRH fragment. These were compelling human pharmacology results for that specific albumin-binding molecule. They were not clinical trials of CJC-1295 No DAC, and they did not establish improvements in physical performance, tissue healing or lifespan. [7]

A separate study by Ionescu and Frohman used frequent blood sampling to study GH pulses under sustained DAC-CJC-1295 stimulation. The investigators found that pulsatility persisted while hormone secretion increased. This helped clarify physiology, but again investigated the albumin-binding form rather than the No DAC peptide and assessed endocrine measurements rather than patient-important health outcomes. [8]

> A result obtained with **albumin-binding CJC-1295** cannot be copied into a pharmacokinetic claim for **modified GRF(1-29) without DAC**.
>
> **EVIDENCE INTERPRETATION**

This distinction cuts in both directions. It would be unwarranted to assume the shorter molecule produces a days-long response because the DAC conjugate did. It would also be unwarranted to claim that an unmeasured "short pulse" must be safer, more physiological or more effective. Those propositions require direct comparative data that the cited studies do not supply.

CHAPTER 03 / THE EVIDENCE STORY

Ipamorelin earns its own chapter

The compound-specific human record is more informative than a generic description of “ghrelin mimetics.”

Ipamorelin emerged in the 1990s as investigators sought a peptide that could trigger GH release while limiting certain additional pituitary-adrenal signals observed with older secretagogues. Raun and colleagues tested it in rat pituitary cells and studied hormonal selectivity in swine. In those experimental systems, ipamorelin triggered GH release while ACTH and cortisol did not rise significantly beyond comparison responses to GHRH. That was a notable selectivity result within the tested conditions - not a universal safety guarantee for humans or every endocrine endpoint. [4]

A second milestone followed in 1999. Gobburu and colleagues measured ipamorelin concentrations and GH responses in healthy volunteers, fitting a pharmacokinetic-pharmacodynamic model to the data. The study documented a short terminal disposition phase in human plasma and a concentration-linked GH response. Crucially, it established an acute pharmacological response, not a validated regimen for chronic administration or evidence that any long-term symptom or body-composition endpoint improves. [5]

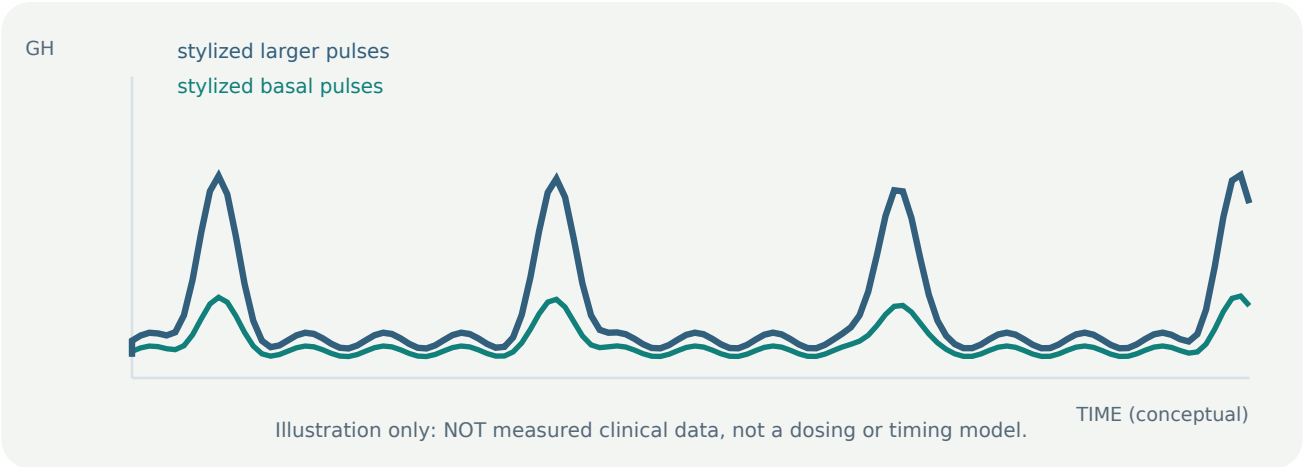


FIGURE 03. Stylized hormone pulses are included solely to explain why GH measurements require repeated sampling. Curves do not reproduce Gobburu et al. or any trial and are not a schedule.

Why hormone peaks are not enough

A GH peak is a real measurement. The difficulty comes when it is translated into broader claims. Circulating GH changes rapidly; downstream IGF-I behaves differently; different organs respond according to local receptor density and metabolic context. Even a repeatable increase in a hormone does not prove muscle gains, fat reduction, improved sleep, faster recovery or enhanced longevity. Those outcomes require controlled trials measuring those endpoints, ideally over an appropriate follow-up period. [5,7,8]

Researchers must also separate the direct actions of a ghrelin-receptor agonist from downstream actions mediated by GH. Ghrelin receptors participate in gastrointestinal and neuroendocrine signaling; a signal measured in the pituitary is only one part of the molecule's biology. The ipamorelin literature therefore extends into gut motility and animal skeletal studies, but positive findings there cannot be read as established human outcomes. [9-13]

A CAREFUL READING OF “SELECTIVE”

Raun et al. studied selectivity under particular experimental conditions. “Selective GH secretagogue” does not mean “free of other effects,” “risk free,” or “safe in every population.”

CHAPTER 04 / THE EVIDENCE STORY

The human studies: what was actually learned

Human research contains real endocrine signals, one important negative clinical result and a conspicuous missing combination trial.

Consider five frequently cited studies in chronological order. In 1990, healthy men demonstrated dual-pathway synergy with GHRH and GHRP-6. In 1999, a human volunteer study established ipamorelin's hormone-exposure relationship. In 2006, investigators showed sustained GH and IGF-I changes with DAC-bearing CJC-1295, and a separate physiological study described preserved GH pulsatility with that same long-acting compound. Those experiments tell us that particular receptors and peptides can change measured hormones in people. None was designed to determine whether the No DAC/Ipamorelin blend changes a meaningful clinical endpoint. [3,5,7,8]

The fifth study is especially useful because it reminds readers what happens when an attractive mechanism meets a practical endpoint. In 2014, Beck and colleagues reported a multicentre, randomized, double-blind trial of ipamorelin versus placebo in patients recovering from bowel resection. The investigators enrolled 117 patients; 114 formed the safety and modified intent-to-treat populations. The key question was how quickly patients tolerated a standardized solid

meal. The numerical direction of the result favoured ipamorelin, but neither that main analysis nor the secondary efficacy analyses showed a statistically significant difference from placebo. [9]

This was not a study of sleep, body fat, muscle growth or the CJC combination. It tested postoperative gastrointestinal recovery with ipamorelin alone. Nevertheless, it provides an unusually clear cautionary tale: biologically interesting effects can fail to translate into a demonstrable improvement in humans. [9,12,13]

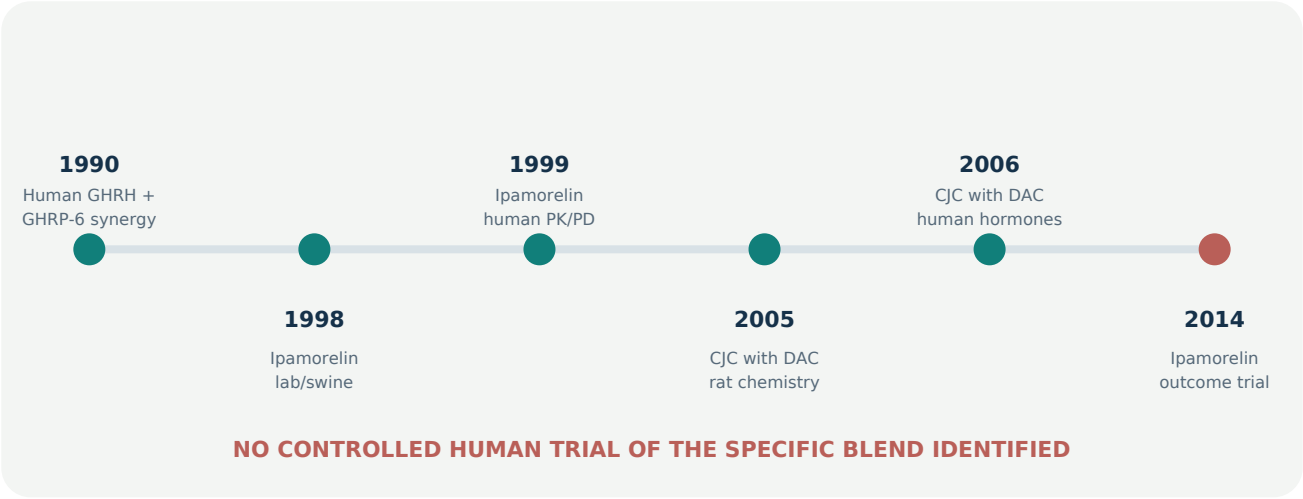


FIGURE 04. A compact timeline of pivotal discoveries. The red note flags the central limitation of extrapolating this literature to a specific marketed combination.

An honest evidence matrix

Research question	Closest direct evidence	What it cannot establish
Two pathway synergy	18 men: GHRH + GHRP-6 [3]	Specific No DAC + ipamorelin blend
Ipamorelin releases GH	Human PK/PD volunteers [5]	Long-term benefit or optimal use
CJC-1295 sustains GH/IGF-I	DAC-bearing human trials [7,8]	No DAC pharmacokinetics or outcomes
Ipamorelin improves bowel recovery	Controlled surgical trial: not significant [9]	Benefit in other clinical populations
Named blend improves health	No controlled human trial identified	Any specific therapeutic efficacy claim

The table deliberately does not assign a clinical benefit score to the blend. Available findings concern different ligands, different populations and different endpoints. A combination cannot inherit all favourable results from each component while discarding inconvenient findings.

CHAPTER 05 / THE EVIDENCE STORY

What animals revealed - and what they did not

Preclinical experiments deserve attention precisely because they reveal mechanisms under controlled conditions.

There is genuine experimental substance behind interest in ipamorelin. In 1999, Johansen and colleagues studied adult female rats and reported changes in longitudinal bone growth under their experimental conditions. A related 2000 study assessed bone mineral content in adult female rats exposed to ipamorelin or GHRP-6. Those papers were not clinical trials and did not establish improved bone strength, lower fracture risk or safety in humans. [10,11]

Such studies can be biologically informative because bone and cartilage are responsive to GH/IGF signaling. But species differences matter: growth plates, endocrine states and the pace of bone remodeling differ between rodents and adult people. Even when an animal outcome is real, the result must be retested with human-appropriate endpoints before it supports a clinical conclusion.

The gut story: a preview of the translation problem

In a 2009 rodent model of postoperative ileus, investigators found that ipamorelin shortened the time to the first bowel movement. Importantly, not every measured parameter moved: cumulative fecal output, food intake and weight gain were not improved in that early observation window. A later animal experiment also examined postoperative gastric emptying with a ghrelin-mimetic approach. These experiments justified asking a larger clinical question; they did not answer it. [12,13]

The 2014 controlled human trial was the real-world test of that line of reasoning. Patients and clinicians cared about recovery of oral intake and gastrointestinal function, not solely receptor engagement. The negative main analysis illustrates why animal models are launching points, not substitutes for direct human evidence. [9,12,13]



FIGURE 05. Evidence ladder. Each rung answers a different question. Positive receptor, animal or endocrine findings cannot be promoted into an unmeasured clinical outcome.

A separate CJC-1295 animal line

Researchers also used the long-acting DAC version of CJC-1295 in a mouse model lacking endogenous GHRH. That line of work explored how an albumin-binding GHRH analog can restore parts of growth regulation under an engineered deficiency state. It is valuable experimental endocrinology, but the model represents neither routine adult physiology nor the unconjugated No DAC molecule. [14]

THE TRANSLATION LESSON

A good preclinical study establishes a mechanism or phenomenon in a defined model. It cannot independently determine whether a commercial peptide combination has a useful benefit-to-risk profile in humans.

CHAPTER 06 / THE EVIDENCE STORY

The outcomes everyone asks about

The most appealing claims are also the easiest to overstate when the studies measured something else.

Body composition and metabolic health

GH and IGF-I are involved in the regulation of fat and protein metabolism. That biological fact makes body-composition hypotheses understandable. Yet the papers reviewed here for modified GRF(1-29) and ipamorelin do not provide controlled human data establishing that the named combination reduces adiposity, increases strength, improves physical function or meaningfully changes body composition. Hormonal biomarkers are upstream measurements; they are not proof of a body-composition outcome. [3-9]

It is particularly important not to borrow results from treatments for confirmed GH deficiency, from recombinant GH itself, or from different approved and investigational GHRH analogs. Such interventions differ in patient selection, molecular identity, exposure profile and measured endpoints. The endocrine axis is shared; the evidence is not interchangeable.

Sleep, recovery, performance and aging

GH secretion follows a complex sleep-related rhythm, and the GH/IGF axis participates in tissue maintenance. These associations inspire research questions about sleep quality, rehabilitation, exercise adaptation and aging. Association, however, is not intervention evidence. No adequately controlled human trial of the precise No DAC/Ipamorelin combination was identified in the reviewed literature that measured these outcomes. The absence of direct outcome data should be visible to the reader wherever possible applications are discussed.

A useful thought experiment asks which measurements would actually matter: not only a GH pulse after exposure, but objective sleep measures, validated functional testing, metabolic assessments, adverse events and durable changes over time compared with placebo. Repeated claims on websites do not become stronger scientific evidence merely because they are repeated.

Bone, gastrointestinal function and endocrine research

Bone and gut motility are distinctive because compound-specific preclinical research exists for ipamorelin. That gives them stronger mechanistic grounding than unmeasured lifestyle claims, while also giving researchers a direct reminder of the animal-to-human translation gap. The controlled gastrointestinal study did not show statistically significant benefit, and the bone experiments were in rats. [9-13]

> What makes the science interesting is not a list of promised outcomes. It is the opportunity to design experiments that can **separate a hormone signal from a genuine improvement in health.**
>
> EVIDENCE INTERPRETATION

CHAPTER 07 / THE EVIDENCE STORY

Safety is a research question, too

Changing a hormone pathway and proving that a human intervention is safe are separate tasks.

The GH/IGF axis participates in glucose regulation, fluid balance and tissue growth. A study that measures a temporary hormone response cannot settle the long-term effects of repeated receptor stimulation. Potential concerns worth investigating include altered glucose handling, edema or fluid retention, headache, tingling symptoms, changes in endocrine feedback and effects that might matter in populations with pre-existing conditions. These are plausible monitoring domains, not a claim that the particular blend has been shown to cause each one. [5,7-9]

Likewise, absence of serious events in a small early pharmacology study is not proof of safety over months or years. Rare events require larger populations; cumulative endocrine effects require longer observation; groups such as adolescents, pregnant people and people with malignancy or endocrine disorders cannot be assumed to have the same risk. Even the outcome trial of ipamorelin observed a specialized postoperative population, not otherwise healthy adults pursuing general wellness goals. [7,9]

Formulation quality introduces another separate uncertainty. An experimental peptide's sequence, purity and measured content do not by themselves establish sterility, endotoxin control, stability or safety for administration. Nor does a paper on a reference compound prove that a particular supplier's batch contains the same chemical entity. This literature review cannot assess any specific commercial material.

A CANADIAN PUBLICATION NOTE

This paper is general scientific education, not a product-specific dossier, authorization, advertising clearance or medical recommendation. Health Canada considers the total context of a scientific message, including its proximity to product sales and connected pages. Balanced language and a research disclaimer do not guarantee that a linked website presentation will be considered non-promotional. [15,16]

For the same reason, no dose ranges, schedules, reconstitution volumes, routes of self-administration or combination protocols appear here. Published experiments are reported for their scientific findings, not as instructions. Readers should not treat an unknown commercial preparation as interchangeable with research-grade material used in the cited studies.

CHAPTER 08 / THE EVIDENCE STORY

The experiment that still needs to be done

A strong hypothesis is valuable because it tells us how to design a falsifiable trial.

A well-designed research program would begin with a confirmed molecular definition of "No DAC" modified GRF(1-29), independently verified identity and quality, and validated analytical measurements. It would separately characterize ipamorelin and the actual mixture rather than assuming that knowledge of individual compounds fully predicts combined stability, absorption or receptor interactions.

A controlled human study designed to isolate combination effects would need meaningful comparison groups - including placebo and each constituent alone - with prespecified hormone, metabolic, safety and clinically relevant outcomes. Randomization, masking, sufficiently representative participants and appropriate follow-up would make it possible to distinguish receptor synergy from placebo effects, background GH fluctuations and changes unrelated to the intervention. These are research design principles, not proposed protocols for personal use.

Importantly, researchers should measure both early biology and real-world effects. Repeated GH measurements could characterize endocrine response patterns; IGF-I would provide a related but different readout. Glucose-related measures and adverse-event surveillance would be crucial safety domains. If the scientific question concerned physical function or body composition, trials would need credible direct measurements of those endpoints rather than inferring them from a serum hormone change. Longitudinal observation would be necessary to assess durability.

A rigorous negative result would be informative, too. The experience with ipamorelin in postoperative ileus demonstrates that a plausible pathway can be a productive scientific lead even when a particular therapeutic hypothesis does not survive testing. [9]



FIGURE 06. A future evidence program must move deliberately from molecular identity through exposure and endocrine effects to controlled clinical outcomes.

CHAPTER 09 / THE EVIDENCE STORY

What the evidence supports today

The most reliable scientific conclusions are the ones that retain their original context.

Supported in the cited literature: GHRH and older GHRP-family ligands can stimulate GH through distinct but interacting pathways. Ipamorelin has demonstrated GH-releasing pharmacology in animals and healthy human volunteers. Albumin-binding CJC-1295 with DAC has altered GH and IGF-I in controlled human pharmacology studies. Certain ipamorelin animal models have shown bone-related or gut-motility responses. [3-8,10-14]

Not established for the named combination: direct human pharmacokinetic behavior, the magnitude or persistence of two-peptide synergy, improvements in sleep, muscle mass, fat loss, athletic recovery, bone outcomes or healthspan, and long-term safety. The lack of a controlled human blend study is the central limitation, not a minor caveat. The 2014 ipamorelin postoperative study also reminds us that a biological rationale can coexist with a negative clinical trial. [9]

A reader could reasonably leave this literature with genuine curiosity. Two receptor systems are involved; early human experiments with related ligands show that endocrine responses can be amplified; compound-specific ipamorelin pharmacology is documented. But curiosity is not a clinical endpoint. The intellectually honest next step is better research rather than a larger claim.

> The right conclusion is neither “it works” nor “nothing is known.” It is that **the mechanisms are worth investigating, while the specific combination remains clinically unproven.**
>
> **EDITORIAL CONCLUSION**

SCOPE OF THIS REVIEW

The synthesis prioritizes published original studies indexed in PubMed and regulatory materials available through 26 October 2026. It is a narrative selection, not a systematic review or meta-analysis. No unpublished private study, particular commercial product or batch was evaluated.

SOURCE LIBRARY / CLICKABLE PRIMARY REFERENCES

Where the evidence comes from

The numbering corresponds to citations in the text. Sources [1-14] are original investigations; [15-16] are official Canadian regulatory guidance. Links lead to the primary journal record, PubMed record or government publication.

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