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Tirzepatide:
Safety, Efficacy, and Delivery Approaches

Whitepaper

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Executive Summary

Tirzepatide is a dual agonist of the glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptors, designed to target key pathways involved in glucose metabolism and appetite regulation. Clinical studies demonstrate that tirzepatide is a well-tolerated obesity intervention that is associated with significant reductions in body weight (often approaching 20%), as well as improvements in appetite regulation, waist circumference, body composition, and cardiometabolic risk profiles. At Fridays, our tirzepatide products leverage this dual GIP/GLP-1 mechanism to support appetite control through both subcutaneous injection and in our liposomal delivery methods that make oral use possible, improving convenience and consistency. The StatRX delivery system, in particular, enables a needle-free option that allows for reliable absorption. Overall, Fridays' tirzepatide products provide a safe and effective way to support appetite regulation, metabolic efficiency, healthy weight management, and overall wellness.

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Table of Contents


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GLP-1/GIP
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1 Introduction

Obesity is a rapidly escalating global health issue, with more than 40% of American adults classified as obese in 20221. Obesity is associated with a wide range of serious health complications, including type 2 diabetes, high blood pressure, cardiovascular disease, nonalcoholic fatty liver disease, and increased risk of several cancers, ultimately resulting in reduced quality of life and increased mortality[2].

Standard strategies for obesity management, including changes in diet, increased physical activity, and behavioral changes, often fail to produce substantial or sustained weight loss for many individuals[3]. The limited long-term effectiveness of lifestyle modification alone has underscored the urgent need for more effective, evidence-based, and medically supported approaches to weight management.

In response to this unmet need, incretin-based therapies, most notably glucagon-like peptide-1 (GLP-1) receptor agonists and dual incretin receptor agonists, have emerged as promising therapeutic options for the treatment of obesity[4]. These therapies target key pathways involved in appetite regulation and glucose metabolism, offering significant and sustained weight loss for many individuals[4–6].

At Fridays, our mission is to provide scientifically grounded, evidence-based healthy weight management solutions. By integrating cutting-edge clinical research with innovative delivery systems and personalized, physician-guided care, Fridays bridges the gap between advanced metabolic science and accessible, real-world treatment options for individuals seeking sustainable improvements in health and wellness.

2 Background and History of GIP, GLP-1, and Tirzepatide

Glucose-dependent insulinotropic polypeptide (GIP), originally named gastric inhibitor polypeptide, is a hormone first identified in the early 1970s, with early research proposing GIP could reduce stomach acid production[7]. Later studies revealed that GIP has a more important role in glucose metabolism by stimulating the pancreas to release insulin in response to food intake. This discovery helped define what is now known as the "incretin effect", where oral food intake triggers a greater insulin response than glucose delivered directly into the bloodstream[8].

GIP is secreted by K cells, which are specialized cells located predominantly in the upper small intestine (duodenum and jejunum) in response to food intake, especially fats and carbohydrates[8]. In addition to its role in insulin release, further research has shown that GIP also plays a role in fat storage and energy balance, and therefore may contribute to the development of obesity and metabolic disease[9]. For many years, GIP was thought to be less viable as a therapeutic target in type 2 diabetes because its effects appeared to be reduced in this population. However, more recent findings demonstrated that the problem is not a loss of GIP receptors, but rather a reduced sensitivity that may be reversible, thereby renewing interest in GIP as a therapeutic target[10].

GLP-1 was identified in the 1980s as a hormone produced from the proglucagon gene. GLP-1 is secreted by L cells found mainly in the lower part of the small intestine (ileum) and colon when food is consumed[11]. GLP-1 helps the body manage blood sugar levels by stimulating insulin release, reducing glucagon (a hormone that raises blood sugar), slowing how quickly the stomach empties, and increasing feelings of fullness, making GLP-1 a powerful regulator of both blood sugar control and appetite[12].

As GLP-1 is rapidly degraded by the enzyme dipeptidyl peptidase-4 (DPP-4), this led to the development of longer-acting forms of GLP-1 (GLP-1 receptor agonists) and medications that slow its breakdown (DPP-4 inhibitors)[12]. An agonist is a compound that mimics a natural hormone by binding to the same receptor and activating it to produce a biological response. Both GIP and GLP-1 work by binding to specific receptors, especially on insulin-producing pancreatic β-cells, triggering internal signals that increase insulin release when needed[13]. Together, GIP and GLP-1 are responsible for most of the body's natural incretin response after a meal, therefore forming the biological basis for dual incretin receptor targeting, which aims to improve both blood sugar regulation and weight control.

Tirzepatide is a first-in-class, dual agonist of both the GIP and GLP-1 receptors. It was initially developed for the treatment of type 2 diabetes mellitus but, more recently, it has been used as an effective therapeutic option for weight management[11].

2.1. Tirzepatide Mechanism of Action

Tirzepatide is a 39-amino acid synthetic peptide that acts as a dual agonist of both GIP and GLP-1 receptors, which play important roles in insulin secretion, appetite regulation, and metabolic control[14]. Although its structure is based on GIP, tirzepatide is specifically

designed to activate both GIP and GLP-1 receptors. It contains a side chain that promotes reversible albumin (protein in the blood) binding, thereby slowing its breakdown and allowing for once-weekly dosing[14].

Tirzepatide stimulates insulin secretion from pancreatic β-cells and decreases glucagon release from α-cells, helping to lower both fasting and post-meal blood sugar levels[15]. Additionally, it slows gastric emptying and affects appetite-regulating centers in the brain, which reduces food intake, increases feelings of fullness, and supports weight loss[11].

Tirzepatide acts as an agonist at both GIP and GLP-1 receptors and is often referred to as a 'twincretin'[15]. It has a stronger effect on the GIP receptor than on the GLP-1 receptor, which may enhance its metabolic benefits[16]. Through its dual-receptor activity, tirzepatide may lead to improved blood sugar control, reduced appetite, enhanced feelings of fullness, improved insulin sensitivity, and significant weight loss[11] (Figure 1). Compared with traditional GLP-1 receptor agonists alone, tirzepatide has been shown to be more effective for blood sugar management and weight reduction[5,17–19].

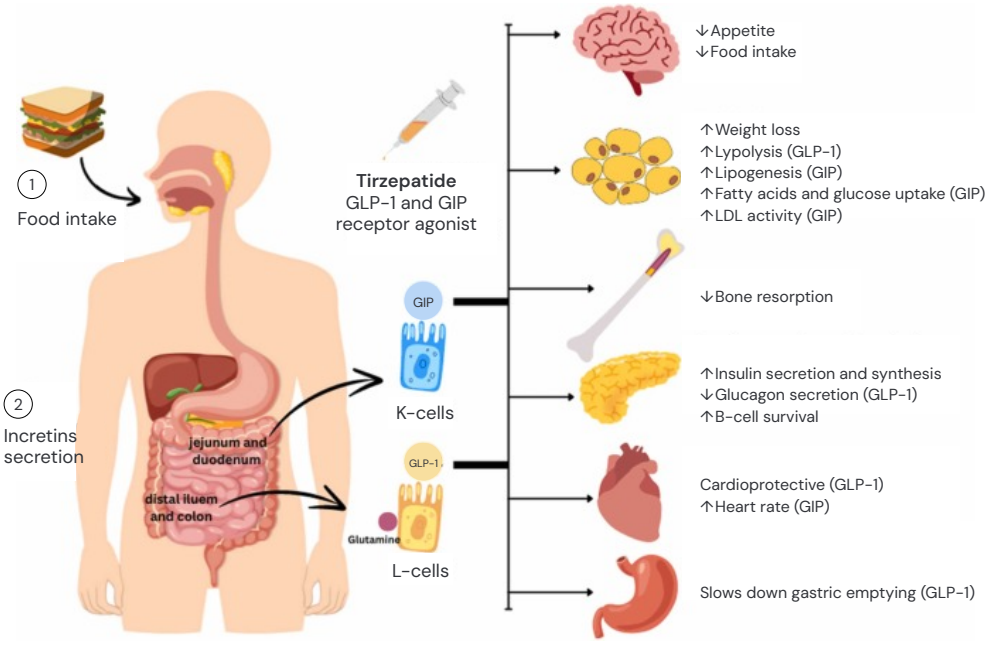

Figure 1. Mechanism of action of tirzepatide. Image from Sokary and Bawadi, 2025[11]. Image used under Creative Commons License.

2.2. Pharmacokinetics of Tirzepatide

After subcutaneous injection, tirzepatide is gradually absorbed into the bloodstream[20]. It binds strongly to albumin, which helps tirzepatide stay in the body longer and supports once-weekly dosing[20]. Over time, tirzepatide is broken down into amino acids and eliminated as metabolites in the urine and feces[20,21]. Its long half-life of approximately five days allows for steady, consistent effects throughout the week.

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3 Clinical Data Supporting Tirzepatide

Supplementation with tirzepatide has been evaluated extensively in recent years, with multiple large-scale randomized controlled trials and meta-analyses in populations with obesity and type 2 diabetes. Clinical research is ongoing; however, current evidence suggests that tirzepatide can produce significant reductions in body weight, suppress appetite and food cravings, improve eating behavior, enhance body composition, reduce waist circumference, and improve key cardiometabolic markers[4–6,22–26].

3.1. Significant Reduction in Body Weight

Multiple meta-analyses and systematic reviews have evaluated the clinical efficacy of tirzepatide for weight reduction in populations with obesity and type 2 diabetes[4,5]. In one systematic review and meta-analysis of ten studies involving 9,873 participants with obesity and/or type 2 diabetes, tirzepatide was associated with a significant pooled mean reduction of body weight of -9.81 kg compared to the placebo[4]. Subgroup analyses further demonstrated that each of the evaluated doses (5 mg, 10 mg, and 15 mg) produced statistically significant weight reductions compared to the control groups[4].

In an additional systematic review comprising data from 5,800 participants enrolled in randomized controlled trials comparing tirzepatide and semaglutide, treatment with tirzepatide (5 mg) was associated with a mean difference in body weight of -12.47 kg compared to those treated with placebo, highlighting the significant weight-loss potential of tirzepatide even at lower dosages[5].

One of the most notable clinical trials investigating tirzepatide is the phase III double-blind, randomized, controlled trial (SUMOUNT-1 trial), which involved 2,539 adults with a body-mass index (BMI) of ≥30 kg/m², or ≥27 kg/m² and at least one weight-related complication, excluding diabetes[6]. Participants received once-weekly subcutaneous tirzepatide (5 mg, 10 mg, or 15 mg) or placebo for 72 weeks, including a 20-week dose escalation period. Substantial and sustained reductions in body weight were observed in participants receiving the 10 mg and 15 mg doses, with mean reductions of approximately 19.5% and 20.9% from baseline, respectively, compared to a mean reduction of approximately 3% in the placebo group (Table 1)[6].

Another noteworthy study is the phase III randomized withdrawal clinical trial (SUMOUNT-4 trial), which was conducted at 70 sites across four countries, involving 783 adults with a BMI of ≥30 kg/m², or ≥27 kg/m² with at least one weight-related complication, excluding diabetes[22]. Participants first completed a 36-week open-label lead-in period during which they received once-weekly subcutaneous tirzepatide at their maximum tolerated dose (10 mg or 15 mg)[22]. At week 36, 670 participants were randomized in a double-blind manner to either continue with tirzepatide treatment or switch to placebo for an additional 52

weeks. Participants who completed the lead-in phase achieved a mean weight reduction of 20.9%. From week 36 to week 88, those who continued tirzepatide treatment experienced an additional mean reduction in body weight of 5.5%, whereas those who switched to the placebo regained a substantial proportion of the weight lost[22]. These findings underscore the importance of continued tirzepatide treatment to maintain and further augment initial weight loss.

When compared with GLP-1 receptor agonists, multiple trials and meta-analyses report that participants treated with tirzepatide achieved significantly greater reductions in body weight compared to those treated with semaglutide[5,17–19].

Together, these studies demonstrate that tirzepatide significantly reduces body weight, supports superior weight-loss outcomes compared to other GLP-1 receptor agonists, and highlights the importance of continued treatment for long-term maintenance of weight loss.

*Table 1. Summary of the body weight results from the SURMOUNT-1 trial. Adapted from Forzano et al., 2022[23], used under Creative Commons License. * = p<0.001*

Outcomes		Tirzepatide 5 mg (n = 630)	Tirzepatide 10 mg (n = 636)	Tirzepatide 15 mg (n = 630)	Placebo (n = 643)
Body Weight (Kg)	Baseline	102.9	105.8	105.6	104.8
	From baseline (%)	−15	−19.5	−20.9	−3.1
	Versus placebo (%)	−11.9 *	−16.4 *	−17.8 *	

3.2. Improved Body Composition and Waist Circumference

A sub-study of the SURMOUNT-1 trial evaluated body composition changes in a subset of 160 participants (tirzepatide pooled doses, n = 124; placebo, n = 36) selected from the original cohort of 2,539 individuals[27]. Participants underwent dual-energy X-ray absorptiometry scans at baseline and at Week 72 to assess changes in body composition[27]. From baseline to Week 72, participants treated with tirzepatide experienced a mean reduction in body weight of -21.3%, fat mass of -33.9%, and lean mass of -10.9%, compared with a -5.3% reduction in body weight, a -8.2% reduction in fat mass, and a -2.6% lean mass reduction in the placebo group[27]. Of the total body weight lost, approximately 75% was attributable to fat mass and 25% to lean mass in both treatment and placebo groups[27].

In addition, significant reductions in waist circumference were observed in the main SURMOUNT-1 trial among participants receiving tirzepatide. Those treated with 15 mg and 10 mg demonstrated mean reductions of -17.7 cm and -18.5 cm from baseline, respectively, whereas the placebo group had a reduction of -4.0 cm[23] (Table 2).

*Table 2. Summary of the waist circumference results from the SURMOUNT-1 trial. Adapted from Forzano et al., 2022[23], used under Creative Commons License. * = p<0.001*

Outcomes		Tirzepatide 5 mg (n = 630)	Tirzepatide 10 mg (n = 636)	Tirzepatide 15 mg (n = 630)	Placebo (n = 643)
Waist circumference (cm)	From baseline	−14	−17.7	−18.5	−4
	Versus placebo	−10.1 *	−13.8 *	−14.5 *	

3.3. Appetite Suppression and Improved Eating Behavior

A six-week, phase I clinical study involving 114 adults without diabetes and with a BMI ranging from 27 to 50 kg/m² was conducted to evaluate changes in energy intake and ingestive behavior following treatment with tirzepatide or placebo[24]. Changes from baseline to week 3 were assessed using standardized meal testing, self-reported measures of appetite and eating behavior, and blood-oxygenation-level-dependent functional magnetic resonance imaging in response to food images[24]. Tirzepatide was associated with a significant reduction in energy intake compared to placebo at week 3, with an estimated treatment difference of -524.6 kcal. In addition, participants receiving tirzepatide reported decreases in overall appetite, food cravings, perceived hunger, tendency to overeat, and reactivity to food cues in the environment[24]. Neuroimaging analyses demonstrated reduced activation in response to high-fat, high-sugar food images in several brain regions, including the medial frontal and cingulate gyri, orbitofrontal cortex, and hippocampus[24]. These findings suggest that tirzepatide may reduce food intake, potentially by modulating neural and behavioral components of ingestive behavior[24].

Additionally, in a secondary analysis of a phase I randomized controlled trial in adults with obesity (BMI between 30 to 45 kg/m²) who underwent diet counselling and were followed for 18 weeks[25]. Treatment with tirzepatide led to significantly greater weight loss of -16.7 kg compared to -8.4 kg in the placebo group[25]. Additionally, tirzepatide significantly decreased food preferences and food craving scores compared to the placebo. These reductions included less liking of high-fat/high-sugar foods and fewer cravings for sweets, starches, and fast-food fats[25].

3.4. Enhanced Metabolic and Overall Health

In addition to supporting significant weight reduction, tirzepatide has demonstrated benefits across multiple markers of cardiometabolic health[26]. A post hoc analysis of the SURMOUNT-1 trial was conducted using a validated atherosclerotic cardiovascular disease (ASCVD) risk prediction model that included modifiable risk factors such as systolic blood pressure, total cholesterol, HDL-cholesterol, presence of type 2 diabetes, antihypertensive treatment, and smoking status[26,28]. The relative reduction in predicted ASCVD risk from baseline to week 72 ranged from -23.5% to -16.4% in the tirzepatide-treated group, compared to an increase of 12.7% in the placebo group[26,28].

Long-term data from a three-year extension of the SURMOUNT-1 study in adults with prediabetes and overweight or obesity further demonstrated substantial metabolic benefits. Tirzepatide treatment was associated with a 94% reduction in the risk of developing type 2 diabetes compared to placebo, and 92% of tirzepatide-treated participants with prediabetes had sustained reversion to normoglycaemia[6,26].

Tirzepatide has also been shown to have favorable effects on blood pressure in multiple clinical studies[23]. Notably, in the SURMOUNT-1 trial, participants treated with Tirzepatide reported a mean reduction in systolic blood pressure of -7.2 mmHg and a mean reduction in diastolic blood pressure of -4.8 mmHg, compared to a mean reduction in systolic blood pressure of -1 mmHg and a mean reduction in diastolic blood pressure of -0.8 mmHg in the placebo group[23] (Figure 2).

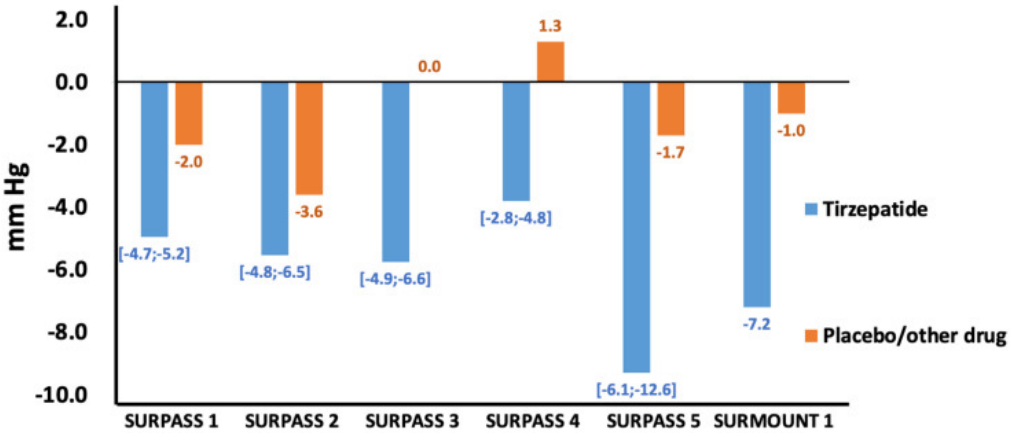

Figure 2. Mean variations in systolic blood pressure (SBP) with tirzepatide vs. placebo/other drugs in clinical trials involving participants with type 2 diabetes or obesity. Adapted from Forzano et al., 2022[23], used under Creative Commons License.

4 Safety and Dosing

Tirzepatide is typically administered between 2.5 mg to 15 mg in 0.5 mL as a once-weekly subcutaneous injection, usually with gradual dose escalation to improve tolerability. Clinical trial data indicate that tirzepatide is generally well-tolerated, with most adverse events being mild to moderate and occurring during the initial dose escalation period[6].

The most commonly reported side effects are gastrointestinal, including nausea, diarrhea, abdominal pain, vomiting, acid reflux, and constipation[29]. Other side effects include injection-site reactions and increased risk of mild hypoglycemia[29,30]. More serious but much less common side effects may include pancreatitis, cholelithiasis, and cholecystitis[30].

Drug-drug interactions may occur when tirzepatide is used in combination with other GLP-1 receptor agonists; therefore, concurrent use is not recommended. In addition, as tirzepatide delays gastric emptying, it may reduce the absorption and systemic exposure of certain oral medications that rely on intestinal uptake, such as acetaminophen and oral hormonal contraceptives[31]. Tirzepatide may also decrease gastric acid and gastrin secretion, which could affect the absorption of medications that require a specific stomach pH to dissolve properly[31].

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5 Fridays' Tirzepatide

Fridays focuses on safety, education, and accessibility, helping individuals explore physician-guided wellness options that may support healthy weight management. With transparent pricing and personalized care, Fridays makes advanced therapies approachable and convenient from home.

Tirzepatide Subcutaneous Injection: Direct delivery of tirzepatide into adipose tissue, where it is gradually absorbed into systemic circulation, providing steady exposure and reducing the need for clinical supervision.

Tirzepatide StatRx Sublingual Delivery: A cutting-edge delivery system now enables tirzepatide to be taken sublingually, encapsulating tirzepatide for potentially enhanced absorption and therapeutic effects. The StatRX delivery system, available exclusively at Friday's, enables easy and reliable delivery of tirzepatide through the sublingual pathway, without the need for needles. Fridays' oral tirzepatide is blended with B12 and L-carnitine, formulated as a combined approach that may support appetite management, metabolism, and sustained energy.

5.1. Tirzepatide Microdosing

Standard clinical administration of tirzepatide typically starts with 2.5 mg weekly, gradually escalating to a maintenance dose. This approach highlights the value of lower-dose exposure in supporting tolerability and long-term adherence. Clinical trial data indicate that tirzepatide is generally well-tolerated at 2.5 mg to 15 mg in 0.5 mL, with most adverse events usually occurring during the primary period of dose escalation[6]. Therefore, maintaining treatment at lower doses for longer periods may be beneficial in reducing the likelihood of adverse events. Clinical trials are currently underway to establish the safety and efficacy of microdosed semaglutide (GLP-1 agonist) through oral and subcutaneous delivery[32].

Microdosing strategies may also offer several other potential benefits. In individuals undergoing multiple treatment or lifestyle changes, initiating therapy at lower doses may improve tolerability and allow for closer monitoring of treatment response[33]. Microdosing may also be useful during planned treatment interruptions, where gradual and controlled reintroduction of tirzepatide could minimize adverse effects while maintaining therapeutic momentum[33].

While formal clinical evidence specific to tirzepatide microdosing is still emerging, its potential applications highlight a promising area for further research and clinical innovation, particularly within personalized weight-management strategies.

6 Conclusion

Tirzepatide represents a scientifically grounded and clinically supported approach to the management of obesity and related metabolic conditions. By targeting both the GIP and GLP-1 receptors, tirzepatide addresses key physiological drivers of weight gain, including appetite dysregulation, impaired glucose control, and metabolic inefficiency. Clinical evidence has demonstrated that tirzepatide produces significant reductions in body weight, as well as improvements in appetite regulation, body composition, waist circumference, and cardiometabolic risk factors[4–6,22–26] (Figure 3). These studies highlight tirzepatide as a potential solution for weight management and also broader metabolic health support.

Across large randomized controlled trials and meta-analyses, tirzepatide has demonstrated a safe and tolerable profile comparable to that of existing incretin-based therapies, with adverse events primarily mild to moderate and most commonly gastrointestinal. As traditional oral delivery methods for peptide-based therapies present limitations due to degradation and poor absorption, advanced delivery technologies are improving accessibility and convenience. Fridays' innovative approaches, including subcutaneous injection and StatRX sublingual delivery, are designed to support reliable absorption while reducing barriers to use. Offering greater flexibility, improved adherence, and improved accessibility.

Taken together, current clinical evidence supports tirzepatide as a safe, effective option for supporting healthy weight management, appetite suppression, and metabolic health. With the added benefits of advanced delivery systems and physician-guided care, Fridays offers a science-backed and patient-focused solution for individuals seeking sustainable improvements in weight management, appetite suppression, metabolic function, and overall wellness.

	People with obesity without T2D
Bodyweight reduction	-16.4 to -24.5%
Waist curcumference	-13.6 to -14.8%
Improved SBP	-6.9 to -9.2 mmHg
Improved DBP	-3.8 to -5.5 mmHg
Improved HDL-C	2.6 to 11.4%
Improved LDL-C	-7.6 to -11.5%
Improved triglycerides	-21.2 to -28.0%
Improved HbA1c	-0.3 to -0.5%

Figure 3. Summary of the effects of tirzepatide from clinical studies involving participants with obesity without type 2 diabetes. Adapted from Sattar et al., 2025[26], under Creative Commons License.

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7 References

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