


Application of Polyglycolic Acid/Poly (Lactic-co-glycolic Acid) in Thread Embedding Acupuncture for Obesity: New Strategies and Challenges

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Abstract: Obesity has become a prominent global public health concern, leading to the development of numerous diseases such as cardiovascular diseases, type-2 diabetes mellitus (T2DM), cancer, and several system diseases. In recent years, thread embedding acupuncture (TEA) has gained popularity as a novel and promising approach to obesity management. This method extends the traditional principles of acupuncture by embedding absorbable threads such as polyglycolic acid (PGA) and poly (lactic-co-glycolic acid) (PLGA) into acupoints. Currently, there has been no review of TEA in obesity management applications. This review is to discuss the clinical applications, mechanisms, new strategies and challenges of PGA/PLGA thread embedding acupuncture in obesity treatment. We conducted a comprehensive search of PubMed, Web of Science, and Embase databases using keywords such as thread embedding acupuncture, acupoint catgut embedding, obesity, and obese, covering the period from inception to 2024. Clinical studies have shown that TEA could significantly reduce weight, waist circumference, and appetite in obese patients. The therapy could modulate systemic inflammation and enhance adipocyte metabolic capacity. Additionally, TEA regulates gut microbiota composition and impacts neuroendocrine pathways, enhancing hypothalamic function and appetite control via leptin receptor activation and energy homeostasis modulation. Despite its therapeutic potential, there are challenges, such as no standard rules for acupoint selection, embedding depth, and treatment frequency. Herein, we suggest the advancements and limitations of PGA/PLGA thread embedding acupuncture. It points out its use for solving problems in obesity treatment and its chance to become a practical and new method in clinics.

Keywords: PGA, PLGA, thread embedding acupuncture, obesity, mechanism

Introduction

Obesity and its related diseases have become a significant global health concern and are recognized as the world's fifth leading cause of death. The World Health Organization (WHO) describes obesity as "an abnormal or excessive accumulation of fat that may impair health". It states that "the root cause of obesity and overweight is an energy imbalance between calories consumed and calories expended".¹ Epidemiological study shows a dramatic increase in obesity rates between 1990 and 2021 at the global, regional and national levels. Compared with 1990, global obesity rates in 2021 increased by 155.1% for males and 104.9% for females.² According to the "World Obesity Report 2024",³ there were 2.2 billion overweight or obese adults in 2020. By 2035, it is projected that nearly 3.3 billion (54%) adults will be overweight or obese. Annually, five million deaths from non-communicable diseases are linked to overweight or obesity. Obesity is a multifaceted health challenge, influenced by genetic and behavioral factors, as well as significant environmental causes such as unhealthy social eating habits and food deserts.⁴ At its core, obesity involves an imbalance of energy intake and expenditure. Positive energy balance leads to weight

gain.⁵ Energy regulation involves intricate physiological interactions, including gut sensory-motor activities, signaling by peripheral hormones, and neural pathways both peripheral and central.⁶

Common obesity treatments include lifestyle changes, medications, and surgery. However, it's typical for individuals to regain weight after modifying their lifestyle. Stopping weight loss medications often leads to weight rebound, with long-term use posing safety concerns. Surgical interventions are limited by their high upfront costs, potential for severe complications, and about 20%-25% of patients experiencing significant weight regain within a year.⁷ This weight rebound may be attributed in part to the metabolic memory of obesity. After significant weight loss or metabolic improvement, multiple cell types in adipose tissue (eg, adipocytes, adipocyte progenitors, and endothelial cells) retain gene expression differences from the obese period. In particular, metabolism-related genes (eg, IGF1, LPIN1, IDH1) remained downregulated after weight loss.⁸ Consequently, innovative treatments are essential to curb obesity's rise. Thread embedding acupuncture (TEA), also known as long-term acupoint stimulation, merges contemporary technology with traditional acupuncture techniques. Embedding absorbable threads into acupoints extends the effects of acupuncture. A meta-analysis⁹ of six clinical trials found that TEA outperformed sham TEA in reducing body weight, body mass index (BMI), waist circumference, hip circumference, and percent body fat. Recognized for its therapeutic benefits,^{10,11} this technique has reduced treatment frequencies from twice weekly to twice monthly.¹² Its cost-effectiveness and time efficiency make TEA an appealing option for obesity treatment.^{13,14} However, adverse events of foreign body cystic granuloma and abscess after TEA have been reported,¹⁵ which often uses primitive catgut threads. Recently, biodegradable threads like Polyglycolic acid (PGA) and poly (lactide-co-glycolide; PLGA) have been increasingly used in TEA due to their higher safety and improved user experience. PGA and PLGA could break down in the body into easily metabolized monomers.¹⁶ Recent studies have demonstrated the potential of TEA using PGA/PLGA.¹⁷ This new approach holds promise for the treatment of obesity. However, clinical practice has revealed efficacy differences in different patients. These issues become existing challenges for this therapy. This paper discusses the clinical applications of PGA and PLGA, particularly their use and mechanisms in TEA for obesity, and discusses their new strategies and challenges in obesity treatment.

Clinical Applications of PGA and PGLA

During the 1960s and 1970s, research on absorbable surgical sutures demonstrated the excellent biocompatibility and biodegradability of PGA and PLGA materials. It led to the wide use of biodegradable materials. Today, these materials are used in absorbable surgical sutures, drug delivery carriers, fracture fixation devices, tissue engineering scaffolds, and suture reinforcement materials (Figure 1).

Absorbable Surgical Sutures

PGA is a linear aliphatic polyester. It features a simple structure with a controllable hydrolytic degradation process. It has gained recognition in the medical field for its use in absorbable sutures, exemplified by the commercial Dexon suture series. In the body, PGA is broken down by enzymes, notably those with esterase activity.¹⁸ Its degradation product, glycolic acid (GA), is non-toxic and is expelled from the body as water and carbon dioxide via the tricarboxylic acid cycle.¹⁸ Research indicates that PGA sutures lose half their strength within two weeks, all their strength in four weeks, and are fully absorbed within four to six months.^{19,20} PLGA, another polymer suture developed commercially, has a higher lactic/glycolic acid ratio to slow down degradation. Edlich et al²¹ reported that PGA sutures cause minimal inflammation compared to other sutures and excel in handling, tensile strength, knot security, non-toxicity, and minimal tissue reaction. PGA does not interfere with the wound healing process and the material is well tolerated in both clean and contaminated procedures. Similar findings have been reported by other researchers.^{22,23}

Drug Delivery Systems

Polyesters are favored in drug delivery systems due to their biocompatibility, biodegradability, processability, and tunable release rates.²⁴ PLGA, in particular, is frequently used clinically in several FDA-approved devices.²⁵ PLGAs as drug carriers can release drugs in a controlled manner. It could offer numerous therapeutic benefits such as eliminating frequent dosing and allowing precise control over drug release rates. Furthermore, it protects active drugs from

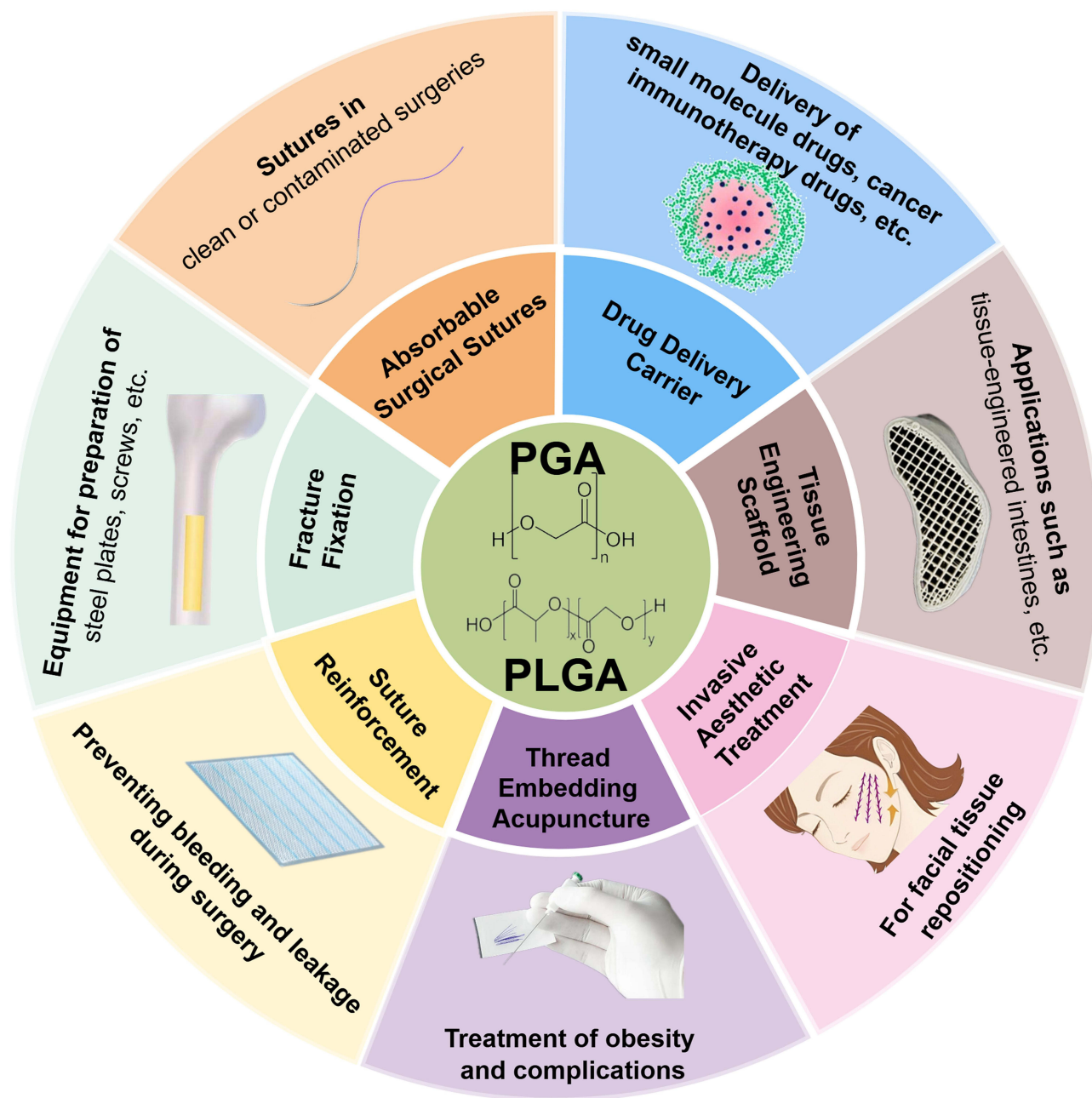


Figure 1 Clinical applications of PGA and PLGA.

degradation before administration and minimizes toxic effects due to fluctuations in drug plasma concentrations.²⁶ Currently, PLGA is applied in delivering small-molecule drugs like ciprofloxacin,^{27–29} and cancer chemotherapy drugs like doxorubicin and paclitaxel.^{30,31}

Fracture Fixation Materials

In orthopedics, biodegradable copolymers are extensively used to make devices like fixation rods, plates, screws, and suture fixators. These materials are employed in enhancing musculoskeletal tissue repair, serving as scaffolds to support tissue growth and as carriers for tissues or cells.^{32–34} For example, devices such as pins and screws are used for bone fixation, and suture anchors are used for anterior cruciate ligament reconstruction. Moreover, cartilage regeneration technologies that use autologous cartilage grafts, chondrocytes, or mesenchymal stem cells are also prevalent. These

polymers, designed as carriers or fillers, directly foster the development of cartilage regeneration technologies. These biodegradable scaffolds are appropriately designed for implantation of articular chondrocytes or progenitor cells.

Tissue Engineering Scaffolds

Tissue engineering scaffolds are important in disease treatment. It provides essential mechanical support for cell attachment and tissue development. Optimal scaffolds meet specific architectural, mechanical, physicochemical, and biological criteria. PGA has been extensively utilized as a scaffold material in tissue engineering. Neurotube™ (Synovis Micro Companies Alliance, Birmingham, Alabama, USA) is a PGA-based neural scaffold device that has been commercialized for both experimental and clinical use.³⁵ These PGA tubes collapse after implantation and are biodegraded and absorbed in the body. Finkbeiner et al³⁶ confirmed that the extracellular matrix alone does not suffice to guide human embryonic stem cells toward differentiation into the endoderm or intestinal lineage. In contrast, PGA scaffolds seeded by human intestinal organoids thrive in the body and develop into tissues nearly identical to mature intestinal tissues. Currently, PGA is applied in scaffolds for nerve repair and reconstruction, oral and craniofacial regeneration, and tissue-engineered intestinal scaffolds.^{37–39}

Suture Reinforcement Materials

PGA can be used to cover wounds, preventing bleeding and leakage during surgery. In certain procedures (such as early-stage oral or oropharyngeal cancer surgeries), the resulting wounds are often too large for primary closure and require coverage with grafts or patches made from various biomaterials. Investigators reported the utility of covering post-surgical wounds of the oral cavity and pharynx with fibrin glue-adhesive PGA sheet.⁴⁰ Covering the wound with a PGA sheet is simpler and less time-consuming than taping, implanting, or using other artificial materials, and it avoids microvascular graft reconstruction. Takeshi Shinozaki et al⁴¹ reported that covering oral cancer surgical wounds with PGA sheets reduced postoperative pain. Currently, PGA sheets are used for fistula closure during lung surgery,⁴² hemostasis in liver surgery,⁴³ dural repair in spinal surgery,⁴⁴ and defect coverage after oral cancer resection.⁴⁰

Other Uses

Beyond these applications, PLGA is used in facial cosmetic surgery. The FDA-approved, minimally invasive absorbable suture treatment known as InstaLift (Sinclair Pharma) is utilized for mid-facial tissue repositioning. These sutures are made of PLGA and other copolymers. The structure of the suture is designed to mechanically support tissues while also promoting gradual and sustained tissue regeneration through collagen stimulation, thus restoring facial contours.⁴⁵ Similarly, products containing PLGA and related polymers (sold in Europe as Silhouette Soft by Sinclair Pharma) have been shown to induce Type I collagen synthesis, effectively doubling the diameter of the filaments within 12 months. This collagen build-up can persist for up to 24 months when the sutures begin to degrade. These sutures are employed for treating mild to moderate skin laxity in the mid-face, lower face, full face, neck, and eyebrow repositioning.^{45,46} In recent years, PGA and PLGA have gained popularity in TEA for obesity. The following discusses its applications and mechanisms in this field.

Thread Embedding Acupuncture

Acupuncture has a long history and unique therapeutic characteristics. It regulates bodily functions through physical stimulation rather than medication. Focusing on a holistic approach, acupuncture influences the body's Qi, blood flow, and meridians by stimulating specific acupoints. Guided by traditional Chinese medicine's diagnostic theories, treatment involves selecting different acupoints based on the underlying causes and symptoms. Acupuncture also exhibits bidirectional regulation, adjusting bodily functions according to individual conditions to restore balance. Acupuncture can be used to treat various conditions, including pain, internal diseases, gynecological disorders, and neurological conditions.^{47–49} However, the typical treatment frequency is 2–3 sessions per week, which poses a significant time challenge for many patients. Recently, long-duration acupuncture techniques have gained popularity, such as press needle therapy, acupoint injections, and TEA. Press needles involve inserting a fine needle vertically into the skin and securing it with tape for 1 to 5 days. During this time the patient can move freely without any discomfort. This method provides

continuous stimulation to the area, enhancing therapeutic effects. It is currently used in treating insomnia, post-stroke hemiplegia, and postoperative recovery.^{50–52} Acupoint injection delivers medication directly into acupoints or tender points. This technique is widely applied to manage diabetic complications, chemotherapy side effects, and knee osteoarthritis.^{53–55}

TEA is an extension and development of acupuncture. It is based on the theory of acupuncture and combines modern medical technology. This technique works by embedding biodegradable threads (such as catgut, PGA, or other materials) into specific acupoints to provide long-term stimulation. The therapy offers sustained acupoint stimulation lasting several days or even weeks, creating a “long-lasting acupuncture effect” characterized by gentle, continuous, and beneficial stimulation. TEA reduces the need for frequent clinical visits. It avoids repeated needle punctures, resulting in less pain. It is particularly suitable for those apprehensive about needles, thereby improving patient compliance. The threads are fully absorbable and non-toxic, making it a safe and eco-friendly treatment. As the threads are broken down and absorbed in the body, they provide physiological, physical, and chemical stimulation to the acupoints, promoting the body’s self-repair and regulatory functions. Its applications are extensive, covering a range of conditions from pain-related and functional disorders to chronic diseases. Additionally, TEA is also applied in cosmetic fields for spot removal, wrinkle reduction, and health-enhancing purposes like anti-aging and boosting immunity.

Thread Embedding Acupuncture for Obesity

Acupuncture has been established as an effective alternative therapy for treating obesity.^{56,57} It could influence hypothalamic, sympathetic, and parasympathetic nerve activities, as well as obesity-related hormones. A meta-analysis⁵⁸ reviewed the efficacy of acupuncture in obesity management. This analysis demonstrated that acupuncture significantly reduces BMI, body weight, body fat mass, and lipid levels compared to sham acupuncture. Studies suggest that acupuncture may modulate the gut-brain axis, thereby affecting dietary behaviors and the gut microbiome.⁵⁹ It is believed to enhance energy expenditure by increasing the browning of adipose tissue, boosting muscle blood flow, and alleviating hypoxia.⁶⁰ Acupuncture may also influence metabolic syndrome in obesity by decreasing inflammation and regulating levels of reactive oxygen species.⁶¹ Recent research suggests that acupuncture’s effects on obesity might involve neuroendocrine modulation, potentially affecting metabolism and appetite control through its action on the hypothalamus and autonomic nervous system.⁶²

As an innovative form of acupuncture, TEA offers enhanced therapeutic effects.^{63,64} A meta-analysis^{11,65} of 33 studies involving 2685 patients with obesity showed that TEA was more effective than acupuncture in reducing BMI (MD = -1.12, 95% CI: -2.09, -0.14) and waist circumference (MD = -2.14, 95% CI: -4.22, -0.06). Its acting mechanism combines traditional acupuncture theory with modern material science. The embedded threads are continuously degraded at the acupuncture points to produce mild physical and biochemical stimulation. It modulates adipose tissue inflammation and induces browning of white adipose tissue to promote adipose metabolism. In addition, it could also regulate intestinal flora, repair intestinal barrier function, and improve leptin/insulin resistance. Multiple mechanisms work together to achieve the regulation of reduced energy intake and increased consumption.

Clinical Study of Thread Embedding Acupuncture for Obesity

We searched PubMed, Web of Science, and Embase databases from inception to 1 October 2024. Our primary search terms included TS1= “thread embedding acupuncture” OR “acupoint catgut embedding” OR “acupoint embedding” OR “catgut embedding”, and TS2= “obesity” OR “overweight” OR “obese” OR “weight loss”. We screened the articles for title and full text. Seven relevant clinical studies were finally obtained. Table 1 summarizes the existing clinical trials of TEA.

Liang et al⁶⁵ conducted a randomized, single-blind, sham-controlled clinical trial involving 84 overweight and obese adults. Participants received TEA or sham TEA every 10 days for a total of 8 sessions. From baseline to the end of treatment, the weight loss in the TEA group was significantly greater than in the sham group (2.97 kg vs 1.40 kg, net difference: 1.57 kg, 95% CI: 0.29–2.86, $p = 0.012$). The superior weight loss effect persisted during a 3-month follow-up period (3.84 kg vs 0.65 kg, net difference: 3.20 kg, 95% CI: 1.17–5.21, $p = 0.001$). Compared to sham therapy, TEA also improved triglyceride levels and reduced subcutaneous fat tissue. One participant in the TEA group reported mild discomfort and tingling after the intervention, with no other adverse events recorded. Similarly, a trial by Xia et al involving 216 subjects demonstrated that TEA effectively reduced both body weight and waist circumference in obese patients.⁶⁸

Table 1 Clinical Study of TEA in the Treatment of Obesity

Years	Sample Size	Obesity Type	Comparison	Thread Material (Length)	Frequency (Duration)	Acupoints	Refs.
2014	99	Obese women	Acupuncture with moxibustion (Acupuncture needles were inserted to a depth of approximately 1–2 cm), long needle acupuncture (6 cun length needles were inserted at CV6, CV12, and ST25 acupoints to a depth of approximately 10–12 cm) with moxibustion, electroacupuncture (dispersed-dense wave at 4 Hz high-density frequency), electroacupuncture with moxibustion and sham acupuncture (stainless-steel needles covered with a plastic film and a cap).	NA	Once per three weeks (6 weeks)	CV6, CV12, ST25, ST36, SP6	[63]
2018	90	Obese women	Sham thread embedding acupuncture (Acupoints were the same as in the test group, but no threads were placed in the syringe needles)	PGA (1cm)	Once a week (6 weeks)	CV6, CV9, ST28, KI14, ST36	[66]
2019	51	Obesity	Lifestyle management (Participants were required to modify their lifestyle and perform the protocols of diet control and physical exercise)	PGA (2cm)	Once per 10 days (10 weeks)	(I) CV12, CV9, CV6, CV7, CV5, KI16, KI14, ST23, ST25, ST27, SP14, SP15, GB26; (II) CV11, CV10, CV4, KI18, KI17, KI15, KI13, ST24, ST26, ST28, SP15, SP160, GB26	[67]
2022	84	Overweight/obesity	Sham thread embedding acupuncture (Acupoints were the same as in the test group, but no threads were placed in the syringe needles)	PDO (1cm)	Once per 10 days (80 days)	CV12, ST25, ST40, BL20	[65]
2022	216	Middle-Aged Obesity	Sham thread embedding acupuncture (Acupoints were located 1 cun away from those of the test group, but no threads were placed in the syringe needles and deqi sensation was not achieved)	PGA (2cm)	Once per two weeks (16 weeks)	(I) TE6, ST25, BL21, ST36, CV12; (II) LI11, ST24, BL20, ST40, CV9	[68]
2023	123	Abdominal obesity	Sham thread embedding acupuncture (Acupoints were located 1–2 cun away from those of the test group).	Collagen (2cm)	Once per three weeks (12 weeks)	BL20, BL21, BL25, CV12, ST25, LR13	[64]
2024	82	Central obesity during perimenopause	Sham thread embedding acupuncture (Acupoints were the same as in the test group, but no threads were placed in the syringe needles)	PDO (1cm)	Once per three weeks (8 weeks)	CV11, CV10, CV9, CV3, SP15, ST25, ST29	[69]

Li Shu et al⁶⁷ assessed 51 obese patients divided into a TEA group and a lifestyle management group. The TEA involved embedding PGA threads at abdominal acupoints every 10 days for a total duration of 10 weeks. The results showed that, compared to baseline, TEA significantly reduced weight, BMI, hip circumference, waist circumference, waist-to-hip ratio, waist-to-height ratio, and abdominal subcutaneous fat thickness ($p < 0.01$), while lifestyle changes only indicated a trend of weight reduction ($p < 0.05$). In addition, TEA improved assessment scores in physical functioning, self-esteem, and sexuality. It decreased the levels of blood pressure, blood glucose, LDL, uric acid, and TNF-alpha, IL-1 β , and increased HDL ($p < 0.05$). The trial also indicated that TEA is safe, with tolerable levels of pain and discomfort.

Iju et al⁶⁶ randomized 90 women with abdominal obesity to a TEA group or a sham group. Treatments were conducted once per week for six weeks. Post-treatment, the TEA group showed greater reductions in weight (-1.65 kg vs -0.38 kg, $p < 0.001$) and waist circumference (4.84 cm vs 1.68 cm, $p = 0.04$). Trends also indicated decreases in triglycerides and glycated hemoglobin, with a significant reduction in the leptin-to-adiponectin ratio (3.0 ± 4.8 to 1.9 ± 1.6 , $p = 0.043$). No severe adverse events were reported.

Xin et al⁷⁰ evaluated the effect of TEA on appetite in obese patients. A total of 122 obese participants were divided into two groups, each receiving six treatments over 12 weeks with a four-week follow-up. Among participants with high appetite levels, the appetite scores in the TEA group significantly decreased from a baseline of 7.78 to 5.00 at 16 weeks ($p < 0.05$), compared to a lesser reduction in the sham group. For participants with moderate appetite levels, no significant differences were observed between the groups ($P > 0.05$). The study revealed the nuanced impact of TEA on appetite, reducing it significantly in those with strong appetites without over-suppression. It indicates the potential of TEA as a sustainable strategy for managing obesity.

Yuanyuan et al⁶⁹ discovered that TEA increased the diversity of gut microbiota in perimenopausal women with central obesity. Notably, there was an increase in Kosakonia and Klebsiella after treatment, which showed a negative correlation with weight and waist circumference.

Operation and Acupoints of Thread Embedding Acupuncture for Obesity

Originally, catgut was primarily used for TEA. It provides strong stimulation and frequently leads to adverse reactions. PGA and PLGA, as a new type of thread material for TEA, have gained increasing popularity in recent years for treating obesity. Compared to catgut, PGA/PLGA has a lower incidence of adverse effects,⁷¹ better patient acceptance, and addresses the limitations of current treatments. Typically, PGA/PLGA thread embedding involves a folding technique. The thread is doubled at the needle's tip, ensuring that the lengths of the thread inside and outside the needle are equal. This method simplifies the procedure: the thread is inserted into the acupoint and folded over, continuing deeper until the thread enters the skin outside the hole and then exits the needle directly. Pushed deeper until all of the thread enters the skin, and then the needle is removed (Figure 2A and B).⁷²

The treatment cycle for TEA clinical trials typically lasts 6 to 12 weeks, with treatment frequency once every one to two weeks. Laboratory studies have shown that PGA materials degrade significantly faster by the seventh day. The lactic acid to glycolic acid ratio in PLGA, typically set at 1:9, critically influences its degradation rate.⁷³ Notably, many studies overlook the long-term effects of TEA, often lacking extended follow-up. However, Tang Zuoyang et al⁷⁴ performed a one-year follow-up, demonstrating that TEA can effectively maintain weight loss long-term. There is no standardized depth for embedding in current clinical practice. Some studies have used ultrasound guidance to compare the effectiveness of embedding at different depths for obesity. Results indicate that embedding in the muscle layer is more effective in reducing BMI and waist circumference compared to embedding in the fat layer.⁷⁵ However, muscle-layer embedding produces stronger stimulation and increases patient discomfort. The appropriate depth for embedding remains an open question in clinical settings.

Acupoints commonly used for embedding include Zhongwan (CV12), Qihai (CV6), Shuifen (CV9), Tianshu (ST25), Zusanli (ST36), and Pishu (BL20), primarily located in the abdomen, lower legs, and back (Figure 2C). In Traditional Chinese Medicine, abdominal acupoints are traditionally associated with regulating gastrointestinal functions and addressing local issues, which correspond to excessive abdominal and visceral fat deposition. The selected acupoints on the lower limbs and back are believed to enhance metabolic functions.⁵⁶ The connections between acupoints, meridians, and internal organs suggest that these points not only correspond physiologically with their associated organs but also regulate visceral diseases

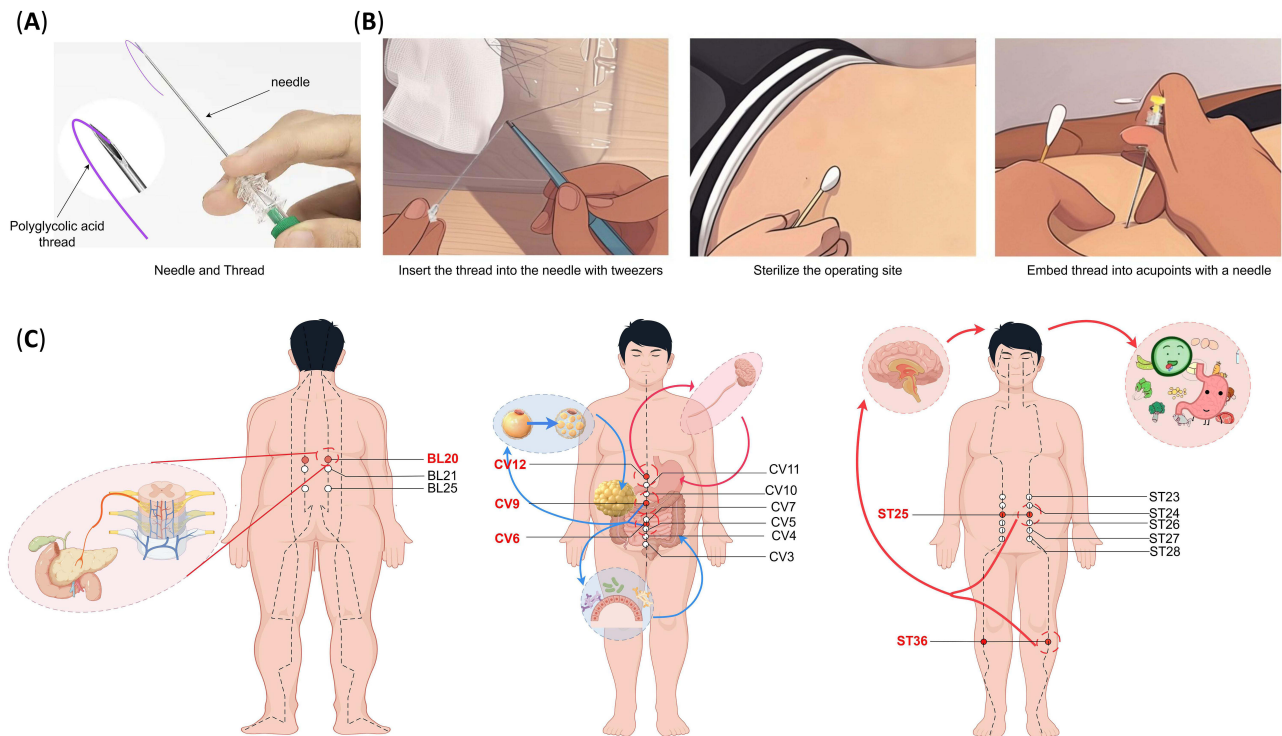


Figure 2 (A) Needle and thread of TEA. (B) Operation of TEA for obesity. (C) Connections of acupoints to organs and tissues for weight loss.

in pathological states (Figure 2C).⁷⁶ A study has identified a dorsal vagal complex (DVC)-vagus nerve-stomach pathway connecting the stomach with CV12. Visceral and somatic afferent impulses converge in the spinal cord, brainstem, and even the hypothalamus. Stimulating CV12 could regulate gastric motility, an effect closely related to the DVC. This stimulation enhances gastrointestinal hormones, thereby modulating gastric motility via the vagus nerve.⁷⁷ Therefore, the function of CV12 is primarily linked with the stomach. CV6 and CV9 are more frequently used for intestinal diseases,⁷⁸ due to their local therapeutic effects. They can improve intestinal epithelial morphology and regulate gut microbiota.⁷⁹ Additionally, they may influence local adipose tissue, promoting fat thermogenesis and thus reducing both subcutaneous and visceral abdominal fat.^{60,80} Stimulate ST36 could activate the bilateral cerebellum, hemisphere lobule VIII, bilateral Rolandic operculum, and right cingulate gyrus.⁸¹ The Rolandic operculum plays a role not only in emotional processing but also in the taste and visceral sensory systems, in conjunction with the cingulate cortex-Rolandic operculum network.⁸² Furthermore, stimulating ST36 and ST25 promotes the expression of BDNF and POMC+ neurons in the hypothalamus, suppressing appetite and achieving weight loss.⁸³ BL20, positioned below the eighth thoracic vertebra, influences parts of T11 that innervate the pancreas. This means that BL20 afferent fibers can regulate pancreatic functions.⁸⁴ Electroacupuncture at BL20 in T2DM rats has been shown to lower blood glucose and insulin, consistent with segmental nerve innervation theory.⁸⁵

Mechanisms of Using PGA/PLGA Thread Embedding Acupuncture for Obesity

The mechanisms of PGA/PLGA thread embedding acupuncture for obesity are complex and require further investigation. Current animal studies and clinical trials have revealed potential mechanisms, related to reducing inflammation, boosting adipocyte metabolism, and altering neuroendocrine functions, ultimately leading to an increase in energy expenditure or a decrease in energy intake (Figure 3).

Modulating Inflammatory States

Obesity is a chronic low-grade inflammatory state,⁸⁶ characterized by significant changes in macrophages during its progression. Specifically, the recruitment of pro-inflammatory M1 macrophages increases, which secrete cytokines like

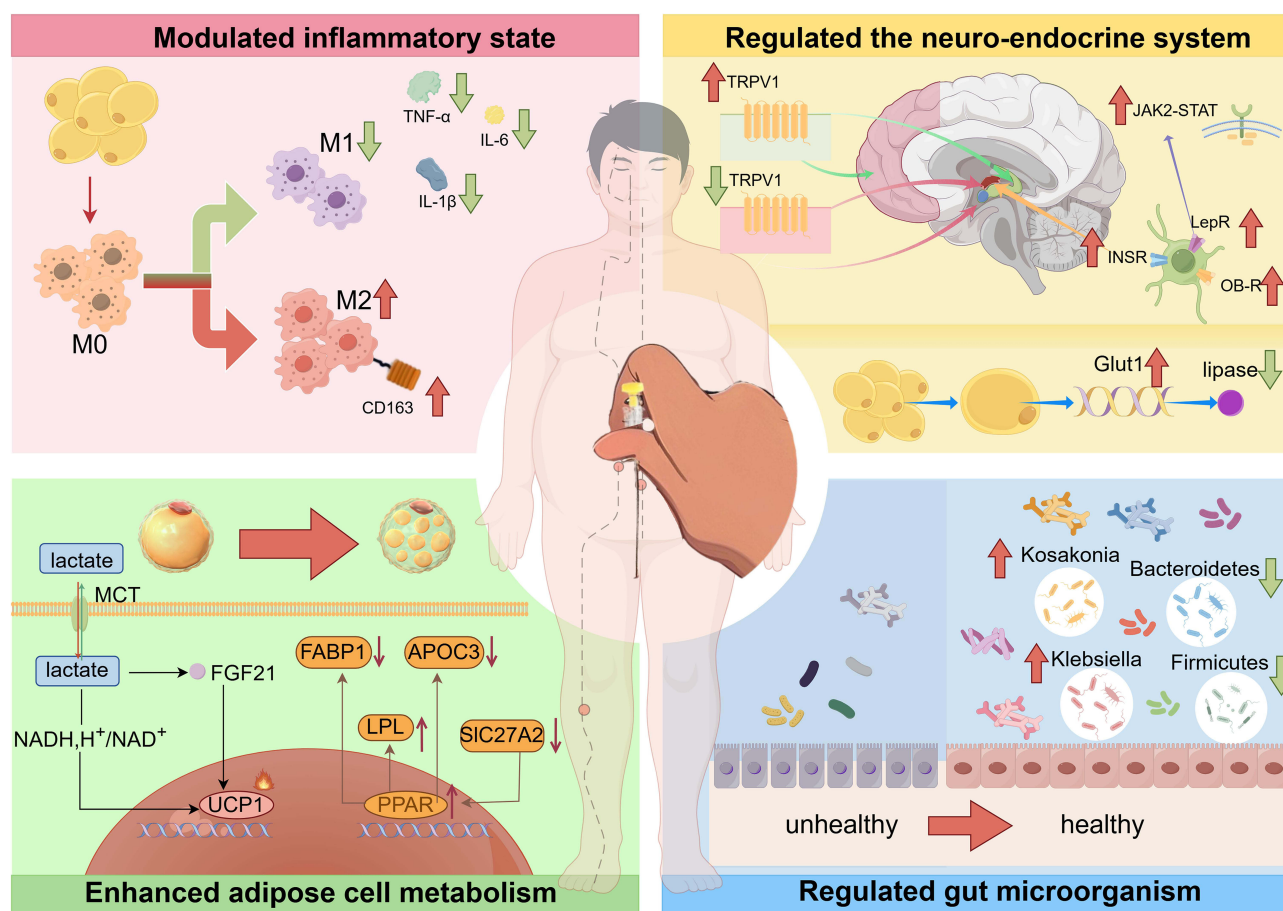


Figure 3 Mechanisms of TEA for obesity.

TNF- α and IL-1 β . An increase in macrophage numbers and the M1-to-M2 macrophage ratio is a hallmark of adipose tissue inflammation in obesity. This inflammation is linked to insulin resistance and the progression of metabolic diseases.⁸⁷

TEA has been shown to inhibit the expression of IL-6, TNF- α mRNA, and MCP-1 mRNA in adipose tissues.⁸⁸ It could reduce inflammation, promotes browning of white fat cells, and enhances thermogenesis and metabolism, thus helping with weight loss.⁸⁹ Additionally, the degradation of PGA/PLGA in the body facilitates this process. PGA degradation products significantly inhibited the production of TNF- α , IL-1 β , and IL-6. The production of TNF- α , IL-1 β , and IL-6 was found to correlate with pH and acid molecules in a macrophage model, and the strongly acidic microenvironment induced by PGA degradation may be a major trigger influencing the inflammatory response.⁹⁰ Moreover, the degradation of PGA fiber implants promotes macrophage polarization to the M2 pro-healing phenotype. When PGA material was implanted subcutaneously in mice, immune cells were encouraged to recruit and activate nearby adipocytes to migrate towards the PGA material, and pro-healing macrophage CD163-positive cells appeared at the implantation site.⁹⁰

Enhancing Adipocyte Metabolic Capacity

White adipose tissue (WAT), one of the largest organs in the body, plays a critical role in energy balance and metabolism. It not only stores excess energy but also secretes various hormones and metabolites that regulate energy homeostasis. Healthy, expandable adipose tissue is essential for metabolic health and preventing triglyceride accumulation in other organs. The downregulation of mitochondrial function or biogenesis in WAT is a central driver of obesity-related metabolic disorders. Mitochondrial functions impaired by obesity affect oxidative capabilities and the renewal and expansion of adipose tissue through the recruitment and differentiation of progenitor cells, negatively impacting overall metabolic health.⁹¹

TEA enhances the metabolic capacity of adipocytes. It regulates the PPAR signaling pathway by upregulating the expression of lipoprotein lipase (Lpl) and downregulating the expression of solute carrier family 27 member 2 (Slc27a2), fatty acid-binding protein 1 (Fabp1), and apolipoprotein C3 (Apoc3), thereby improving fat metabolism in the body.⁹² Following PGA/PLGA implantation, the biodegradation products, lactic and glycolic acids, have recently been identified as effective inducers of browning in white adipose tissue. When PGA/PLGA is implanted, its biodegradation products, lactic acid and glycolic acid,⁷³ play distinct roles in promoting weight loss. Lactic acid has been identified as an effective inducer of WAT browning. Increased lactic acid transport amplifies the expression of thermogenic gene UCP1 in WAT. This process is due to increased MCT transporter activity, elevated intracellular redox stress (NADH/NAD), and upregulated expression of cytokine FGF21.⁹³ Glycolic acid, on the other hand, inhibits lipase activity by reducing the efficiency of 4-NPP oxidation catalysis.⁹⁴ This can reduce the body's fat intake. A clinical trial⁹⁵ showed that human visceral adipose tissue, BMI and waist circumference were negatively correlated with ethanolic acid. At the same time, ethanolic acid levels were lower in the obese population. In summary, the biodegradation products of PGA/PLGA are also beneficial for weight loss.

Regulating the Gut Microbiota

The gut microbiota is the most complex symbiotic microecosystem in the human body, playing a crucial role in metabolism and serving as an important immune barrier. Human health is closely linked to the gut microbial environment. Imbalances in the gut microbiota can lead to obesity. On the one hand, the overall diversity of gut microbiota in obese people is reduced. On the other hand, the intestinal immune barrier is disrupted, leading to the entry of bacterial lipopolysaccharide into the bloodstream and triggering endotoxemia and chronic inflammatory response.⁹⁶ Clinical studies⁶⁹ have shown that TEA can increase the diversity and variation of the gut microbiota in obese patients. Post-treatment, patients exhibited increases in Kosakonia and Klebsiella, which were significantly negatively correlated with weight, waist circumference, and adiponectin levels. After injection of PLGA into obese mice, PLGA is broken down into glycolic acid and lactic acid, which enter the hepatic and intestinal circulations through the liver. This process reduces the cecal pH and alters gut microbiota composition, significantly decreasing the abundance of Bacteroidetes and Firmicutes in the gut.⁹⁷ Glycolic acid is further broken down into glyoxylic acid, which microorganisms use to synthesize substances essential for their growth and reproduction. Therefore, glyoxylic acid may influence gut dysbiosis induced by a high-fat diet.⁹⁸ This mechanism may also explain why PGA/PLGA-based TEA helps improve gut dysbiosis.

Regulating the Neuroendocrine System

The hypothalamus plays a central role in the body's energy balance, containing various neurons that regulate appetite. TEA can improve the transport barriers and post-receptor signaling for insulin and leptin, and reduce lipid peroxidation.⁹⁹ It activates the leptin receptor-mediated Janus kinase 2 (JAK2)/signal transducer and activator of transcription factor 3 (STAT3) signaling pathway in the hypothalamus,¹⁰⁰ and enhances the expression of insulin receptor (INSR) and obesity gene receptor (OB-R) proteins in the hypothalamic arcuate nucleus.¹⁰¹ This modifies central nervous functions, leading to changes in subjective appetite and disrupting energy balance. Additionally, studies suggest that mice fed a high-fat diet showed altered TRPV1 pathway expression in brain regions of the mice: downregulated in the medial prefrontal cortex (mPFC) and hippocampus, and upregulated in the hypothalamus and amygdala, influencing depression-like behaviors and inflammation. By reversing these effects, TEA could increase energy expenditure, reduce food consumption, and improve depressive-like behavior and inflammation in obese mice.^{17,102}

Peripheral tissues also significantly influence obesity and its complications. Experiments have observed that intravenous injection of PLGA in diet-induced obese mice slightly improved glucose clearance rates after a glucose challenge.⁹⁷ Similarly, implanting a PLGA scaffold in the epididymal fat of obese mice reduced fasting blood glucose and improved glucose tolerance, effects similar to those seen after several weeks of treadmill training. Enhanced glucose uptake was observed near the scaffold region.¹⁰³ After scaffold implantation, a new microenvironment formed in the fat tissue, consisting of blood vessels, extracellular matrix, fibroblasts, mononuclear immune cells, and multinucleated macrophages. During scaffold degradation, this microenvironment required large amounts of glucose, thereby reducing fasting blood glucose levels while decreasing adipose tissue size. This effect may be attributed to the degradation of PLGA into glycolic acid and lactic acid. Lactic acid can regulate cellular metabolism,^{104,105} suppress macrophage inflammatory activity, and increase the expression of Glut1 in adipocytes.¹⁰⁶ This finding is particularly promising for obese patients with diabetes. Glut1 facilitates glucose uptake

without requiring insulin or other hormones and induces the expression of glucose transport proteins and local high levels of insulin-like molecules.¹⁰³

New Strategies and Challenges

Despite significant advancements in diagnosing obesity, pharmacological and surgical interventions, adverse effects remain a major challenge in clinical practice. However, the swift progress of traditional Chinese medicine (TCM) for obesity is reshaping the treatment landscape. Unlike conventional methods, TCM focuses on regulating meridians and qi-blood to enhance energy expenditure or reduce energy intake. It places more emphasis on the internal microenvironment and cellular function, improving the patient's quality of life with minimal side effects.¹⁰⁷ Moreover, the high biocompatibility and safety of PGA/PLGA materials have broadened their application in obesity treatment. Current research indicates that these materials do more than stimulate acupoints; they also enhance adipocyte activity through their metabolic processes. Moving forward, the rapid evolution of treatments based on synthetic polymers is setting the stage for the development of effective clinical practices for combating obesity.

Nevertheless, the effectiveness of TCM for obesity varies, demonstrating better results in certain patient constitutions.¹⁴ In addition, the lack of biomarkers to accurately measure treatment efficacy remains the greatest challenge to achieving personalized treatments in precision medicine for obesity, as it is not possible to assess a patient's response to existing treatments. Meanwhile, we must acknowledge that while many clinical studies have yielded meaningful results, those with significantly positive outcomes remain limited. A primary limitation of TEA lies in the absence of standardized treatment protocols, including acupoint selection, embedding depth, and frequency. To address these issues, high-quality clinical research and the establishment of relevant guidelines are essential. Some researchers have already made progress. For example, one RCT involving 216 obese participants yielded positive outcomes 60. Based on these findings, we firmly believe that TEA holds significant potential to address current limitations and drive the rapid development of non-pharmacological obesity treatments in clinical practice. This also represents a primary research direction for the future application of novel polymeric synthetic materials in obesity treatment.

Conclusion

This article introduces PGA/PLGA thread embedding acupuncture as an innovative approach for obesity. With its ease of use, high safety, and long-lasting effects, it has gradually replaced acupuncture as a popular method in traditional Chinese medicine for obesity management. Our study shows multiple clinical studies using PGA/PLGA thread embedding acupuncture for obesity and suggests that it is associated with multiple mechanisms. It mitigates inflammatory states, boosts adipose tissue metabolism, adjusts the gut microbiota, and modulates the neuroendocrine system, collectively aiding in metabolic enhancement and weight reduction. The high biocompatibility of PGA/PLGA materials could promote the future development of TEA for obesity. However, the main challenge of TEA is the lack of standardised treatment protocols, including acupoint selection, embedding depth and frequency. With the advantages of fewer adverse events and higher compliance, TEA is particularly suitable for the long-term prevention and control of obesity. With the advantages of fewer adverse events and higher compliance, acupoint acupuncture is particularly suitable for the long-term prevention and control of obesity. Furthermore, through the precise matching of acupoints and the design of personalised treatment plans, TEA is expected to achieve a breakthrough in the field of obesity precision medicine.

Ethics Statement

This medical review does not require approval from an ethics committee due to its nature and scope. It primarily involves the synthesis and analysis of existing medical literature and research, without conducting any original research studies or clinical trials that would require ethical review. As a result, the ethical considerations that typically apply to research studies do not apply to this medical review.

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