



Parenteral Human Placental Extract and Hydrolysate Therapy: Clinical Applications, Dosing Regimens, Healthy Aging, And Aesthetic Uses — A Scoping Review

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KEYWORDS:

Human placental extract; placental hydrolysate; Laennec; Melsmon; Placentrex; Hominis placenta; injection; healthy aging; menopause; fatigue; mesotherapy.

ABSTRACT

Background: Human placental extracts and hydrolysates have been administered parenterally for several decades, particularly in Japan, South Korea, India, and China, for indications ranging from liver disease and menopausal symptoms to fatigue, musculoskeletal disorders, oral submucous fibrosis (OSMF), healthy aging, and aesthetic dermatology. However, clinical evidence remains geographically dispersed, and formulations, routes, doses, treatment schedules, and follow-up periods are highly heterogeneous.

Objective: To map the human clinical evidence for parenterally administered placental preparations, focusing on clinical indications, formulations, routes of administration, dosing regimens, treatment duration, follow-up, efficacy, and safety, with particular attention to healthy aging and aesthetic applications.

Methods: A scoping review of international and regional literature was conducted from database inception through August 2026, without restrictions on publication language or date. Eligible studies evaluated human placental extract (HPE), human placental hydrolysate (HPH), placental polypeptides, or Hominis placenta administered intramuscularly, subcutaneously, intradermally, intralesionally, submucosally, by pharmacopuncture, or by targeted musculoskeletal injection. Exclusively oral and topical preparations, cellular therapies, and placental membrane products were excluded from the primary synthesis. Data on preparation, dose, injection volume, frequency, cumulative exposure, treatment duration, follow-up, efficacy, and adverse events were extracted and synthesized descriptively.

Results: Clinical studies were concentrated in South Korea, Japan, India, and China. In older adults, eight weeks of subcutaneous HPE significantly improved the between-group change in physical function compared with placebo ($P=0.036$). In a randomized trial involving 108 women with menopausal symptoms, the Kupperman Menopausal Index decreased by 12.30 ± 10.44 points with HPE versus 7.15 ± 9.11 with placebo ($P=0.012$). Another trial involving 84 women demonstrated improvement in menopausal symptoms ($P=0.033$) and increased estradiol concentrations ($P=0.031$) compared with placebo. A placebo-controlled trial involving 78 participants with chronic fatigue reported significant improvements in fatigue measures, particularly in the chronic fatigue syndrome subgroup. In alcoholic or non-alcoholic steatohepatitis, a randomized comparative trial found that a reduction in alanine aminotransferase of at least 20% occurred

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in 62.9% of HPE-treated participants versus 48.8% of comparator-treated participants in the per-protocol population ($P=0.0772$), without demonstrating superiority. A smaller NASH pilot study found significant reductions in aminotransferases at week 8, but not at weeks 12 or 24, and no statistically significant improvement in the NAFLD Activity Score ($P=0.078$). In shoulder impingement syndrome, three weekly ultrasound-guided injections of 4 mL HPH significantly improved pain, disability, and health-related quality of life compared with placebo (all $P<0.001$). In OSMF, intralesional placental extract improved mouth opening and burning symptoms, although combination therapies or active comparators produced greater improvements in some studies. A randomized Chinese study involving 156 adults with sensitive skin demonstrated improvement in facial hemoglobin content and global aesthetic assessment after three intradermal mesotherapy sessions. However, a placebo-controlled pharmacopuncture trial did not demonstrate significant superiority for its primary menopausal hot-flash endpoint. No clinical study demonstrated increased human lifespan or reduced mortality.

Conclusion: Parenteral human placental preparations have demonstrated clinical effects in selected indications, particularly menopausal symptoms, physical function, chronic fatigue, OSMF, and musculoskeletal disorders. Emerging evidence also concerns aesthetic dermatology. Nevertheless, marked heterogeneity in preparations, doses, routes, comparators, and follow-up limits generalization. Current evidence supports further investigation of healthspan-related outcomes but does not establish placental preparations as longevity therapy.

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1. INTRODUCTION

Human placenta is a biologically complex organ containing peptides, amino acids, nucleotides, lipids, carbohydrates, minerals, and numerous other bioactive compounds. Pharmaceutical preparations derived from human placenta have been used for several decades, particularly in Japan, South Korea, China, and India. Depending on the manufacturing process, these products have been described as human placental extract (HPE), human placental hydrolysate (HPH), placental polypeptide preparations, or Hominis placenta [1–4].

Commercially available preparations include Laennec®, Melsmon®, Unicenta®, and Placentrex®. Importantly, these products cannot necessarily be considered pharmacologically interchangeable because differences in extraction, hydrolysis, purification, sterilization, and manufacturing procedures may result in different molecular compositions and biological activities [1].

Experimental studies have demonstrated antioxidant properties of HPE and identified potentially active compounds and collagen-derived peptides [2–4]. Additional experimental evidence suggests anti-inflammatory activity, stimulation of hepatic regeneration, hepatoprotective effects, and modulation of pathways involved in skin and extracellular-matrix homeostasis [5–8]. These findings provide biological plausibility for clinical investigation but cannot, by themselves, establish therapeutic efficacy.

Parenteral placental preparations have been investigated across a remarkably broad range of clinical settings. South Korean studies have evaluated subcutaneous HPE for menopausal symptoms, fatigue, and health-related outcomes in older adults [9–13]. Japanese and Korean studies have investigated placental preparations in chronic liver disease and steatohepatitis [14,15]. Hominis placenta pharmacopuncture has been evaluated in painful and musculoskeletal disorders [16,17], whereas Indian investigators have accumulated substantial experience with intralesional placental extract for OSMF [18–21]. More recently, Chinese investigators have evaluated intradermal placental polypeptide injections for dermatological and aesthetic indications [22].

Interest has also expanded toward healthy aging and aesthetic medicine. Potential effects on physical function, fatigue, inflammation, oxidative stress, tissue repair, skin extracellular matrix, and musculoskeletal function overlap with domains relevant to healthspan. However, improvement in an aging-related functional or biological outcome should not be interpreted as evidence of increased longevity.

Despite decades of use, the clinical literature remains fragmented across countries, languages, medical specialties, and regional journals. Considerable heterogeneity exists in preparation, concentration, route, anatomical injection site, injection volume, frequency, cumulative exposure, treatment duration, and follow-up.

Therefore, this scoping review aimed to map the clinical evidence regarding parenterally administered human placental preparations, with particular emphasis on clinical indications, formulations, routes of administration, dosing regimens, treatment duration, follow-up, efficacy, and safety.

2. METHODS

2.1. Study design

A scoping review approach was selected because of the substantial heterogeneity in clinical indications, placental preparations, routes of administration, dosing schedules, study designs, and outcome measures.

The methodology was guided by established recommendations for scoping reviews and the PRISMA extension for Scoping Reviews (PRISMA-ScR) [23,24].

2.2. Eligibility criteria

Studies were eligible when they investigated a preparation derived from human placenta administered parenterally to human participants.

Eligible routes included intramuscular (IM), subcutaneous (SC), intradermal injection or mesotherapy, intralesional or submucosal injection, pharmacopuncture, and local image-guided or anatomically targeted injection.

Randomized controlled trials, non-randomized comparative studies, prospective and retrospective clinical investigations, and informative clinical series were considered.

Studies exclusively evaluating oral or topical placental products were excluded from the primary clinical synthesis.

Studies involving placental stem cells, cellular transplantation, placental or amniotic membranes, umbilical-cord-derived therapies, or other regenerative products not consisting of placental extract, hydrolysate, or related injectable preparations were also excluded. Preclinical studies were excluded from the clinical evidence tables but were considered for biological and mechanistic context.

2.3. Search strategy

A broad international literature search was conducted across major biomedical databases and regional bibliographic sources, including literature from Japan, South Korea, China, and India. The search strategy combined terms related to placental preparations, including "placenta", "human placenta", "human placental extract", "placental extract", "human placental hydrolysate", "placental hydrolysate", "placental polypeptide", "Hominis placenta", "Laennec", "Melsmon", "Unicenta", and "Placentrex", with terms related to parenteral administration, including "injection", "injectable", "intramuscular", "subcutaneous", "intradermal", "mesotherapy", "intralesional", "submucosal", and "pharmacopuncture". Additional searches incorporated indication-specific terms, including "aging", "healthy aging", "longevity", "fatigue", "menopause", "liver disease", "steatohepatitis", "pain", "oral submucous fibrosis", "alopecia", "hair loss", "skin rejuvenation", and "aesthetic dermatology". Search terms were adapted to the indexing systems and search syntax of individual databases. Reference lists of eligible studies and relevant reviews were also examined to identify additional historical and regionally published reports.

The literature was searched from database inception through August 2026, without restrictions on publication date, language, or geographical location. Studies published in any language were considered eligible for inclusion when sufficient methodological and clinical information could be retrieved.

2.4. Data extraction

For each eligible study, the following information was extracted: author and year, country, clinical indication, study design, participant characteristics, number enrolled and analyzed, preparation, commercial product and manufacturer when reported, concentration, ampoule volume, route and anatomical site, dose or volume per administration, frequency, total number of injections, treatment duration, cumulative exposure when calculable, comparator, primary and secondary outcomes, adverse events, post-treatment observation, and final follow-up. Treatment duration and post-treatment follow-up were recorded separately.

Information that could not be verified from the available source was designated not reported (NR). Dose, concentration, or route was not inferred from usual commercial practice when it was not explicitly documented.

2.5. Evidence synthesis

Because of substantial clinical and methodological heterogeneity, findings were synthesized descriptively and organized by indication. No meta-analysis was undertaken. The clinical findings were grouped into systemic applications, local and musculoskeletal applications, oral submucous fibrosis, aesthetic and dermatological applications, and healthy aging. Particular attention was given to distinguishing statistically significant between-group differences from improvements observed only within treatment groups.

3. RESULTS

3.1. Overview of the evidence

The identified clinical literature was concentrated predominantly in South Korea, Japan, India, and China. The major clinical domains were healthy aging and physical function, fatigue, menopausal symptoms, liver disease, musculoskeletal pain and dysfunction, OSMF, and aesthetic and dermatological applications.

The principal preparations included Laennec, Melsmon, Unicenta, Placentrex, Hominis placenta, and injectable placental polypeptides. Marked differences in composition and administration prevented these interventions from being regarded as pharmacologically equivalent.

Systemic studies generally employed SC or IM administration, whereas local applications included subacromial injection, intradermal mesotherapy, pharmacopuncture, and intralesional or submucosal injection.

The characteristics, treatment regimens, efficacy findings, and safety data of systemic studies are summarized in Table 1. Local and aesthetic applications are presented in Table 2, and OSMF studies are summarized separately in Table 3. An indication-specific synthesis is provided in Table 4.

3.2. Healthy aging and physical function

Kong and Park randomized 40 healthy community-dwelling Korean adults aged 65 years or older to HPE or saline, of whom 39 were included in the final analysis [9].

HPE was administered subcutaneously in the abdomen for eight weeks, using a step-down regimen comprising 12 injections and a cumulative volume of 32 mL.

Physical function, sexual life, and general health perception improved significantly from baseline within the HPE group. More importantly, the mean change in physical-function score differed significantly between HPE and placebo ($P=0.036$) [9].

The study provides preliminary evidence for an effect on a healthspan-related functional outcome but did not evaluate lifespan, mortality, frailty-free survival, or long-term prevention of age-related disease. Furthermore, the short treatment period and absence of prolonged post-treatment follow-up prevent conclusions regarding the durability of the observed functional improvement.

3.3. Menopausal symptoms

Several controlled studies evaluated parenteral HPE for menopausal symptoms [10–13]. Kong et al. randomized 84 Korean women aged 40–64 years with menopausal symptoms and fatigue to SC HPE or placebo [10]. Seventy-eight women completed the study, including 40 in the HPE group and 38 in the placebo group. Participants received Laennec for eight weeks, using 4 mL twice weekly during the first two weeks, followed by 2 mL twice weekly during weeks 3–4 and 2 mL once weekly during weeks 5–8. The cumulative planned exposure was 32 mL over 12 injections. The Menopause Rating Scale score decreased significantly more in the HPE group than in the placebo group ($P=0.033$). Fatigue also improved significantly within the HPE group, according to the Fatigue Severity Scale ($P=0.002$) and visual analog scale ($P=0.001$). Serum estradiol increased significantly compared with placebo ($P=0.031$), whereas cardiovascular risk factors did not show significant changes [10].

Lee et al. subsequently conducted a randomized, double-blind, placebo-controlled trial involving 108 women with climacteric symptoms [11]. Participants received JBP Plamon, containing 100 mg of placental extract per 2mL ampoule, administered subcutaneously three times weekly for four weeks. Ninety-two women completed the study, including 45 in the HPE group and 47 in the placebo group. Although both groups improved, reduction in the Kupperman Menopausal Index was significantly greater with HPE (-12.30 ± 10.44 versus -7.15 ± 9.11 points; $P=0.012$). Significantly greater improvements were also reported for vasomotor symptoms ($P<0.001$), insomnia ($P=0.001$), and weakness ($P=0.035$) [11]. One participant developed urticaria after the first injection and discontinued treatment. Mild and transient adverse events were also reported.

A subsequent multicenter double-blind study compared Unicenta with Melsmon using SC injections for menopausal symptom improvement [12]. Unicenta satisfied the predefined non-inferiority criterion compared with Melsmon. However, this finding does not establish pharmacological equivalence between the products or demonstrate superiority over placebo. Not all findings were positive.

A randomized placebo-controlled study of Hominis placenta pharmacopuncture in 128 peri- or postmenopausal women did not demonstrate statistically significant superiority for the primary hot-flash endpoint [13]. At week 9, the residual hot-flash scores were $47.09 \pm 41.39\%$ in the placental pharmacopuncture group and $56.45 \pm 44.92\%$ in the control group ($P=0.262$). No statistically significant between-group differences were observed in mean changes in Menopause Rating Scale scores, follicle-stimulating hormone, or estradiol.

Taken together, these studies suggest that clinical effects may depend on the preparation, treatment protocol, population, and specific outcome assessed.

3.4. Chronic fatigue

A multicenter, double-blind, placebo-controlled trial investigated SC HPE in 78 participants with chronic fatigue [25]. Participants received HPE or placebo three times weekly for six weeks. Treatment effects differed according to fatigue classification. In the subgroup with chronic fatigue syndrome, HPE produced significantly greater reductions in Fatigue Severity Scale scores

($P=0.0242$), fatigue visual analog scale scores ($P=0.0009$), and Multidimensional Fatigue Inventory scores ($P=0.0159$) compared with placebo. However, statistically significant differences were not consistently demonstrated in the subgroup with idiopathic chronic fatigue. These findings suggest a possible indication-specific effect, but the subgroup results should not be generalized to all individuals with fatigue. The short treatment duration and limited post-treatment observation also prevent conclusions regarding sustained efficacy.

3.5. Liver disease

Choi et al. conducted a multicenter, open-label, randomized comparative study in patients with alcoholic or non-alcoholic steatohepatitis [14]. The intention-to-treat population comprised 194 patients, with 154 available for per-protocol analysis. The primary efficacy criterion was a reduction in alanine aminotransferase (ALT) of at least 20%. In the per-protocol analysis, this endpoint was achieved by 62.9% (44/70) of HPE-treated patients compared with 48.8% (41/84) receiving the active comparator ($P=0.0772$). Thus, a numerical difference was observed, but superiority was not demonstrated. The authors reported that the predefined non-inferiority criterion was satisfied. Nevertheless, non-inferiority for a biochemical endpoint does not establish equivalence in histological or long-term clinical outcomes. Mild-to-moderate adverse drug reactions were reported in 3.1% of participants.

Shimokobe et al. evaluated ten patients with biopsy-confirmed NASH unresponsive to lifestyle intervention [15]. Participants received Laennec 4 mL IM twice weekly for 24 weeks, corresponding to 48 planned sessions and a cumulative volume of 192 mL. Nine patients completed treatment, and seven underwent repeat liver biopsy. Serum aminotransferase activities decreased significantly at week 8 compared with baseline. However, these reductions were no longer statistically significant at weeks 12 and 24. The mean NAFLD Activity Score decreased from 5.29 ± 0.95 to 4.00 ± 1.83 , although this difference did not reach statistical significance ($P=0.078$). Four of seven participants fulfilled the study's definition of histological response. Fibrosis improved in three patients, remained unchanged in three, and progressed in one. No adverse events were reported during the study.

These findings suggest a possible biochemical and histological signal but remain exploratory because of the small sample size, absence of a control group, and limited number of repeat biopsies.

3.6. Musculoskeletal disorders and pain

A randomized controlled trial enrolled 50 patients with shoulder impingement syndrome [16]. Participants received three weekly ultrasound-guided subacromial injections of 4 mL HPH or saline. The cumulative planned exposure was 12 mL. At nine weeks after the final injection, between-group differences significantly favored HPH for pain during activity, total Shoulder Pain and Disability Index score, and EQ-5D-5L utility index (all $P<0.001$). Mean pain during activity decreased from 57.1 ± 13.1 to 20.2 ± 20.1 in the HPH group, compared with 55.2 ± 15.6 to 51.8 ± 25.9 in the placebo group. No severe local infection or clinically relevant laboratory abnormality was reported.

A multicenter randomized trial involving 82 patients with chronic temporomandibular disorder compared Hominis placenta pharmacopuncture with physical therapy [17]. The intervention comprised ten treatment sessions administered twice weekly over five weeks. Improvements were reported in pain and selected functional and quality-of-life outcomes, with follow-up extending to week 25. However, pharmacopuncture involves a specific anatomical and procedural approach, and its results cannot automatically be extrapolated to conventional systemic SC or IM administration.

3.7. Oral submucous fibrosis

The Indian literature contained several studies evaluating intralesional or submucosal placental extract for OSMF [18–21,26]. Goyal et al. studied 160 patients, allocated to four groups of 40 [18]. The Placentrex arm received 2 mL placental extract mixed with 1 mL of 2% lignocaine, administered intralesionally once weekly for 12 weeks. Participants were followed for 12 months. At week 12, the greatest increase in mouth opening occurred with combined Placentrex, hyaluronidase, and dexamethasone (7.30 ± 0.80 mm), followed by Placentrex alone (5.94 ± 0.84 mm), hyaluronidase and dexamethasone (5.11 ± 0.92 mm), and the control group (0.37 ± 0.16 mm). During follow-up, partial loss of the improvement was observed. The greatest relapse in mouth opening occurred in the Placentrex-alone group (1.62 ± 0.45 mm), whereas the combination group showed the smallest relapse (0.20 ± 0.08 mm). These findings indicate that the initial improvement and its durability should be considered separately.

Other comparative studies reported improvements in mouth opening, burning sensation, or mucosal characteristics following intralesional Placentrex, although active comparators were superior in some comparisons [19–21].

Naik et al. conducted a comparative study involving 60 patients with OSMF, randomly allocated to two groups of 30 [26]. Group A received intralesional triamcinolone acetonide 10 mg/mL combined with hyaluronidase 1,500 IU, whereas group B received 2 mL Placentrex intralesionally once weekly for eight weeks. Mean mouth opening increased from 16.27 to 35.90 mm in group A and from 15.83 to 33.80 mm in group B. At week 8, the between-group difference was 2.10 mm (95% CI 1.20–3.00; $P<0.001$), favoring triamcinolone plus hyaluronidase. Both groups showed reductions in oral burning and improvements in mucosal appearance. However, between-group differences were not statistically significant for burning sensation ($P=0.167$) or mucosal appearance ($P=0.960$). No injection-related reactions or complications were reported during the eight-week treatment period. Although the

authors' concluding statement suggested comparable efficacy for trismus, their numerical results demonstrated a statistically significant difference in final mouth opening favoring the active comparator.

Overall, the OSMF literature suggests that intralesional placental extract may improve clinical symptoms and mouth opening, but the magnitude and durability of benefit vary according to the comparator, concomitant treatment, and follow-up duration.

3.8. Aesthetic and dermatological applications

A multicenter randomized Chinese trial enrolled 156 adults with moderate-to-severe sensitive facial skin [22]. Participants were allocated in a 2:1 ratio to placental polypeptide injection or control. The active group received three intradermal mesotherapy sessions of 4 mL per session at 30-day intervals, corresponding to a cumulative volume of 12 mL. The full analysis population comprised 154 participants, including 103 in the intervention group and 51 in the control group. At day 90, the reduction in facial skin hemoglobin content, the prespecified objective primary endpoint, was significantly greater in the intervention group than in the control group (-1705.82 ± 1808.17 versus -756.65 ± 1493.17 ; $P=0.001$). Global Aesthetic Improvement Scale assessment also favored placental polypeptide treatment, with improvement reported in 88.9% of treated participants versus 5.9% of controls ($P<0.001$). However, several secondary objective outcomes, including erythema area, skin roughness, wrinkle score, and dermal thickness, did not differ significantly between groups at day 90. Adverse events were reported in 5.8% of treated participants and 9.6% of controls, without serious adverse events.

These results support further investigation of intradermal placental polypeptides for sensitive skin but do not establish efficacy for generalized skin rejuvenation, prevention of cutaneous aging, or systemic longevity.

3.9. Historical evidence concerning female alopecia

Hauser reported a historical clinical series involving 65 women treated with injectable placental extract for hair loss occurring either during the postpartum period or independently of childbirth [27]. Overall clinical improvement was reported in 74% of participants, while complete recovery occurred in 43%. Among women with postpartum hair loss, improvement and complete recovery were reported in 91% and 64% of cases, respectively.

Although these findings suggest a potential therapeutic effect, the study was not described as a randomized or placebo-controlled trial. The original abstract does not specify the commercial preparation, exact injection route, dose, treatment frequency, duration, follow-up period, or adverse-event profile. Furthermore, the number of participants in the postpartum subgroup and the objective criteria used to define improvement and complete recovery could not be established from the available bibliographic information.

Consequently, these historical findings should be interpreted as preliminary clinical observations rather than controlled evidence of efficacy. The absence of a control group is particularly relevant because spontaneous recovery may occur in postpartum hair loss. Nevertheless, the study represents an early clinical investigation of injectable placental extract for female alopecia and provides historical context for subsequent research on placental derivatives in dermatology.

3.10. Treatment duration and follow-up

Systemic studies generally lasted four to eight weeks, although IM treatment for NASH extended to 24 weeks [15]. A major limitation was that final assessment frequently coincided with treatment completion. Therefore, durability after discontinuation remains uncertain. Longer post-treatment follow-up was available in selected local-injection studies. The shoulder trial followed patients for nine weeks after the final injection [16], and the temporomandibular disorder trial included assessments up to week 25 [17].

In OSMF, follow-up extended to 12 months in the study by Goyal et al. [18], allowing the investigators to document partial loss of the initial improvement. By contrast, Naik et al. evaluated patients during the eight-week treatment period without documenting prolonged post-treatment follow-up [26].

The aesthetic mesotherapy study included a primary assessment at day 90, approximately 30 days after the final treatment session [22].

3.11. Safety

Across the clinical studies, parenteral placental preparations were generally reported as well tolerated during the investigated periods. However, adverse-event reporting varied considerably. In the menopausal trial by Lee et al., one participant developed urticaria after the first injection and discontinued treatment [11]. The shoulder and aesthetic studies did not report serious treatment-related adverse events during their respective observation periods [16,22]. No injection-related complications were reported in the eight-week OSMF study by Naik et al. [26].

Nevertheless, relatively small sample sizes and short follow-up prevent reliable assessment of uncommon adverse reactions or the safety of repeated exposure over years. Safety data obtained with one manufactured product should not automatically be extrapolated to other placental preparations.

4. DISCUSSION

This scoping review demonstrates that parenteral human placental preparations have been investigated across a broad range of clinical indications, with substantial differences in product composition, route of administration, dosing schedules, treatment duration, comparators, and outcome measures.

The clinical evidence is neither uniformly positive nor uniformly negative. Several controlled trials have demonstrated measurable improvements in selected outcomes, whereas other studies have failed to demonstrate superiority over placebo or active comparators. These findings emphasize the importance of interpreting the evidence according to the specific preparation, indication, route, and endpoint rather than treating all injectable placental products as a single therapeutic intervention.

4.1. Biological plausibility and preparation heterogeneity

Human placental preparations contain diverse molecular components, including amino acids, peptides, nucleotides, and other biologically active substances.

Experimental investigations have demonstrated antioxidant, anti-inflammatory, hepatoprotective, and tissue-related biological activities [1–8]. However, differences in extraction, hydrolysis, purification, sterilization, and manufacturing may substantially influence the composition and biological properties of the final product. Consequently, injection volume alone is insufficient to establish dose equivalence between Laennec, Melsmon, Unicenta, Placentrex, Hominis placenta, and placental polypeptide preparations. The biological effects observed in experimental models should also be distinguished from demonstrated clinical efficacy in humans.

4.2. Healthy aging and longevity

Healthy aging represents an important potential area of investigation because several outcomes evaluated in placental-extract studies overlap with domains relevant to healthspan. The trial conducted by Kong and Park demonstrated a statistically significant improvement in physical function among older adults receiving SC HPE compared with placebo [9]. Similarly, studies of menopausal symptoms and fatigue reported improvements in selected patient-reported outcomes [10,11,25]. These findings suggest that placental preparations may influence certain symptoms and functional domains relevant to quality of life. However, healthspan and lifespan are distinct concepts. An improvement in physical function, fatigue, or subjective health status does not establish a reduction in biological aging, prevention of age-related disease, or extension of human lifespan. No clinical study identified in the present synthesis directly evaluated longevity, mortality reduction, or validated biological-aging endpoints.

Future investigations should incorporate objective measures of physical performance, frailty, sarcopenia, cognition, metabolic and inflammatory biomarkers, and validated biological-aging measures. Long-term follow-up would also be necessary to determine whether short-term functional improvements translate into sustained clinical benefits.

4.3. Menopausal symptoms and fatigue

The menopausal literature contains several randomized controlled trials demonstrating improvements in selected symptom scores following SC HPE administration [10–12]. The trial by Lee et al. demonstrated a significantly greater reduction in the Kupperman Menopausal Index compared with placebo [11]. Kong et al. similarly reported improvements in menopausal symptoms and an increase in estradiol concentrations compared with placebo [10]. However, the negative primary hot-flash result of the Hominis placenta pharmacopuncture trial illustrates that efficacy cannot be generalized across all preparations or administration techniques [13].

The fatigue literature also requires careful interpretation. In the placebo-controlled study by Park et al., statistically significant improvements were concentrated in the chronic fatigue syndrome subgroup rather than consistently observed across all participants with chronic fatigue [25]. Moreover, fatigue and menopausal symptom scales are subjective outcomes and may be influenced by placebo effects, baseline symptom severity, and patient expectations.

Future studies should employ standardized diagnostic criteria, validated outcome instruments, appropriate placebo controls, and longer post-treatment follow-up.

4.4. Hepatic applications

The hepatic literature provides evidence of biochemical changes following parenteral placental preparations, but the clinical significance of these changes remains uncertain.

The randomized comparative study by Choi et al. reported that HPE satisfied the predefined non-inferiority criterion for ALT reduction compared with an active comparator [14]. However, superiority was not demonstrated for the primary biochemical endpoint. Furthermore, biochemical improvement does not necessarily establish histological improvement or prevention of clinically relevant hepatic outcomes. The pilot study by Shimokobe et al. demonstrated significant reductions in aminotransferases at week 8, but these differences were no longer statistically significant at weeks 12 and 24 [15]. The reduction in the NAFLD Activity Score also failed to reach statistical significance. Although four of seven participants fulfilled the study's definition of histological response, the uncontrolled design and small number of repeat biopsies substantially limit interpretation.

Larger randomized trials with histological endpoints and prolonged follow-up are required before a disease-modifying effect can be established.

4.5. Musculoskeletal and pain-related applications

The randomized shoulder impingement trial demonstrated statistically significant improvements in pain, disability, and health-related quality of life following ultrasound-guided subacromial HPH injection compared with saline [16]. The magnitude of improvement suggests a clinically relevant signal that warrants independent replication. However, the study evaluated a specific local injection technique in a defined musculoskeletal condition. Its results cannot be extrapolated to systemic IM or SC placental administration or to other chronic pain disorders. Similarly, the temporomandibular disorder trial investigated a specific pharmacopuncture protocol rather than conventional systemic injection [17].

Future studies should distinguish the pharmacological effects of placental preparations from the procedural effects of local injection, pharmacopuncture, and associated interventions.

4.6. Oral submucous fibrosis

OSMF represents one of the most extensively investigated local applications of injectable placental extract in the identified clinical literature. Several comparative studies reported improvements in mouth opening, burning sensation, and mucosal characteristics following repeated intralesional or submucosal administration [18–21,26]. However, the magnitude of benefit varied considerably across studies. The randomized trial by Goyal et al. demonstrated that the combination of Placentrex, hyaluronidase, and dexamethasone produced the greatest improvement in mouth opening at week 12 and the smallest subsequent relapse [18]. The distinction between initial improvement and durability is particularly important because OSMF is a chronic fibrotic condition. The original study by Naik et al. provides additional comparative evidence [26]. Although both treatment groups demonstrated substantial improvement in mouth opening, the combination of triamcinolone and hyaluronidase produced a significantly greater final interincisal distance than Placentrex alone. The absence of significant between-group differences in burning sensation and mucosal appearance suggests that different clinical domains may respond differently to these interventions. The inconsistency between the authors' concluding statement and their numerical results further emphasizes the importance of extracting and interpreting original outcome data rather than relying exclusively on published conclusions.

Future OSMF trials should employ standardized staging, objective measurements, appropriate comparators, and prolonged follow-up to assess relapse and durability.

4.7. Aesthetic dermatology

Aesthetic dermatology represents an emerging area of clinical investigation for injectable placental preparations. The randomized Chinese trial demonstrated a statistically significant reduction in facial skin hemoglobin content and improvement in global aesthetic assessment following intradermal placental polypeptide mesotherapy [22]. These findings are relevant to the management of sensitive facial skin. However, the study employed an open-label design and a no-treatment comparator, which may influence subjective aesthetic assessments. Furthermore, several objective secondary outcomes, including wrinkle score and dermal thickness, did not demonstrate statistically significant between-group differences. Consequently, improvement in sensitive-skin parameters should not be interpreted as proof of generalized skin rejuvenation or reversal of cutaneous aging.

Additional randomized, blinded, placebo-controlled studies are needed to determine whether these preparations influence objective measures of skin aging, elasticity, pigmentation, wrinkles, or long-term tissue remodeling.

Historical evidence also suggests that injectable placental extracts have been investigated for female alopecia. In a clinical series of 65 women, Hauser reported overall improvement in 74% of participants and complete recovery in 43%, with higher response rates among women with postpartum hair loss [27]. However, the absence of a controlled comparison, the possibility of spontaneous postpartum hair recovery, and insufficient reporting of the injection protocol and follow-up prevent definitive conclusions regarding efficacy. These findings support further investigation using standardized preparations, objective hair-growth measurements, appropriate control groups, and prolonged follow-up.

4.8. Safety considerations

The available clinical studies generally reported acceptable short-term tolerability, although adverse-event reporting was heterogeneous. The urticarial reaction leading to treatment discontinuation in the trial by Lee et al. demonstrates that clinically relevant hypersensitivity reactions may occur [11]. The absence of serious adverse events in small or short-term studies should not be interpreted as evidence of long-term safety. Repeated parenteral administration of biological preparations also requires attention to product quality, manufacturing consistency, sterility, and potential immunological reactions. Differences between commercial formulations further limit the extrapolation of safety findings from one product to another. Long-term pharmacovigilance and standardized adverse-event reporting should therefore be incorporated into future clinical investigations.

4.9. Limitations

The evidence base is characterized by heterogeneous preparations, relatively small trials, short follow-up, variable comparators, inconsistent reporting of concentration, and geographically concentrated research. Several historical studies do not meet contemporary reporting standards. In addition, publication bias cannot be excluded. The heterogeneity of the products and clinical indications also makes conventional pooling problematic. For this reason, the scoping-review approach is appropriate, and no overall efficacy estimate should be calculated across all preparations and indications. An additional limitation is that several studies assessed

outcomes only at the end of treatment, providing limited information regarding the durability of clinical improvement. The historical study of injectable placental extract for female alopecia was included on the basis of the available abstract and bibliographic information because the original full text could not be retrieved. Consequently, the exact injection route, preparation, dosage, treatment schedule, follow-up duration, and detailed safety outcomes could not be independently verified.

4.10. Future research

Future studies should report product, manufacturer, processing method, concentration, ampoule volume, dose, route, anatomical site, frequency, total number of injections, cumulative exposure, treatment duration, and post-treatment follow-up.

For chronic conditions and healthy aging, follow-up at 3, 6, and preferably 12 months after treatment would be particularly informative.

Future aging trials should incorporate objective measures of physical performance, frailty, sarcopenia, cognition, metabolic and inflammatory biomarkers, and validated biological-aging measures rather than relying predominantly on subjective health status. Larger, independently conducted, product-specific randomized trials with standardized dosing, objective endpoints, and prolonged follow-up are required to define the clinical role of parenteral human placental preparations.

5. CONCLUSION

Parenteral human placental preparations have been investigated in human clinical studies for several decades, particularly in East and South Asia, using SC, IM, intradermal, intralesional, submucosal, pharmacopuncture, and targeted musculoskeletal administration. Controlled studies demonstrate measurable clinical effects in selected indications, including improvement in menopausal symptom scores, physical function in older adults, selected chronic-fatigue outcomes, pain and disability in shoulder impingement, mouth opening and burning symptoms in OSMF, and objective skin outcomes following intradermal placental polypeptide treatment.

Liver studies demonstrate biochemical improvement in selected settings, although convincing evidence of histological or long-term disease modification remains limited.

The evidence is therefore neither uniformly positive nor uniformly negative. Its interpretation depends strongly on the specific preparation, indication, route, dose, comparator, and outcome. No clinical evidence currently demonstrates increased human lifespan or establishes parenteral placental preparations as longevity therapy. However, the observed effects on physical function, fatigue, tissue-related outcomes, and selected dermatological endpoints provide a rationale for further investigation within the more precise concept of healthy aging or healthspan. Larger, independently conducted, product-specific randomized trials with standardized dosing, objective endpoints, and prolonged follow-up are required to define the clinical role of parenteral human placental preparations.

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Table 1. Clinical studies of systemic parenteral human placental preparations

Study	Indication Design / N	/ Preparation route	and Dose treatment regimen	and Treatment Follow-up	/ Main findings	efficacy Safety Limitations	/
Kong and Park, 2012 [9]	Healthy adults and ≥65 years; single-blind placebo-controlled RCT; 40 randomized, 39	HPE; abdominal SC	4 mL twice weekly × 2 weeks, followed by 2 mL twice weekly × 2 weeks, then 2 mL	8 weeks; no additional post-treatment follow-up reported	Significant between-group improvement in physical function (P=0.036);	Small sample; subjective health status no longeviti endpoints	

	analyzed (HPE 22; placebo 17)		once weekly × 4 weeks; 12 injections; 32 mL total	group improvements in sexual life and general health perception
Kong et al., 2008 [10]	Menopausal symptoms and fatigue; placebo-controlled RCT; 84 randomized, 78 analyzed (HPE 40; placebo 38)	Laennec; abdominal SC	4 mL twice weekly × 2 weeks, then 2 mL twice weekly × 2 weeks, then 2 mL weekly × 4 weeks; 12 injections; 32 mL total	Greater MRS reduction versus placebo (P=0.033); within-group improvements in no significant FSS (P=0.002) and changes in fatigue VAS cardiovascular risk (P=0.001); factors estradiol increased versus placebo (P=0.031)
Lee et al., 2009 [11]	Climacteric symptoms; double-blind placebo-controlled RCT; 108 randomized, 92 completed (HPE 45; placebo 47)	JBP Plamon, 100 mg/2 mL; SC	2 mL three times 4 weeks; weekly × 4 weeks; 12 injections; 24 mL total	KMI change -12.30±10.44 versus -7.15±9.11 with placebo (P=0.012); vasomotor symptoms P<0.001; insomnia P=0.001; weakness P=0.035
Kim et al., 2023 [12]	Menopausal symptoms; multicenter double-blind non-inferiority RCT	Unicenta versus Melsmon; SC	2 mL per injection, three times weekly; six administrations	Approximately 2 weeks of treatment; longer follow-up according to trial protocol
Choi et al., 2022 [13]	Menopausal hot flashes; placebo-controlled RCT; n=128	Hominis placenta pharmacopuncture	2 mL per session, 9 weeks	Unicenta met the No placebo group; predefined non-inferiority criterion does not establish compared with pharmacological equivalence
Park et al., 2016 [25]	Chronic fatigue; multicenter double-blind placebo-controlled RCT; n=78	HPE; SC	Three injections weekly × 6 weeks; exact injection volume NR in this extraction	Primary hot-flash endpoint not significantly different from No serious treatment-related adverse events reported in MRS, FSH, or estradiol
Choi et al., 2014 [14]	Alcoholic/non-alcoholic	Laennec/HPE; SC or IM	Five consecutive days weekly for up to 6 weeks	CFS subgroup: FSS P=0.0242; VAS P=0.0009; MFI P=0.0159 versus placebo; consistent significant effect in idiopathic chronic fatigue subgroup
			Up to 6 weeks; ≥20% reduction	ALT Mild-to-moderate adverse drug

steatohepatitis; open-label randomized non- inferiority trial; ITT n=194; PP n=154	to 6 weeks; dose treatment-period (44/70) HPE versus reactions in 3.1%; escalation assessment 48.8% (41/84) superiority not permitted comparator; demonstrated according to P=0.0772; non- protocol inferiority reported
Biopsy-proven NASH; Shimokobe prospective et al., 2015 uncontrolled pilot; Laennec; IM [15] 10 enrolled, 9 completed, 7 repeat biopsies	Significant AST/ALT reductions at week 4 mL twice weekly 24 weeks; no 8, but not at weeks No adverse events × 24 weeks; 48 additional post- 12 or 24; NAS reported; very planned sessions; treatment follow- 5.29±0.95 to small uncontrolled 192 mL total up reported 4.00±1.83 sample (P=0.078); histological response in 4/7

Abbreviations: ALT, alanine aminotransferase; CFS, chronic fatigue syndrome; FSS, Fatigue Severity Scale; HPE, human placental extract; IM, intramuscular; ITT, intention-to-treat; KMI, Kupperman Menopausal Index; MFI, Multidimensional Fatigue Inventory; MRS, Menopause Rating Scale; NAS, NAFLD Activity Score; NASH, non-alcoholic steatohepatitis; NR, not reported; PP, per-protocol; RCT, randomized controlled trial; SC, subcutaneous; VAS, visual analog scale.

Table 2. Local, intradermal, pharmacopuncture, and musculoskeletal applications of human placental preparations

Study	Indication / Design / N	Preparation and injection route	Dose and schedule	Treatment / Follow-up	Main efficacy findings	Safety Limitations
Kim et al., 2025 [16]	Shoulder impingement syndrome; single-blind placebo-controlled RCT; n=50 (HPH 24; injection placebo 26)	HPH; ultrasound-guided subacromial injection	4 mL once weekly × 3 injections; 12 mL total	Three-week treatment; nine weeks after final injection	VAS during activity, SPADI, and EQ-5D-5L significantly favored HPH (all P<0.001); clinically relevant VAS 57.1±13.1 to laboratory 20.2±20.1 versus abnormalities placebo 55.2±15.6 to reported 51.8±25.9	No severe local infections or relevant laboratory abnormalities reported
Park et al., 2024 [17]	Chronic temporomandibular disorder; multicenter assessor-blinded RCT; n=82	Hominis placenta pharmacopuncture around predefined treatment points	Ten sessions, twice weekly × 5 weeks; 5 mL injected volume in current week extraction	Five-week treatment; follow-up to week 25	Improvements in pain and selected functional and quality-of-life outcomes	Active physical-therapy comparator; technique differs from conventional SC/IM HPE
Shu et al., 2026 [22]	Moderate-to-severe sensitive facial skin; multicenter open-label RCT; 156 randomized; 154 analyzed (103 PPI; 51 control)	Placental polypeptide injection; intradermal mesotherapy	4 mL/session; Three sessions at 30-day intervals; 12 mL total	Three sessions; final assessment at day 90	Facial hemoglobin change -1705.82±1808.17 versus -756.65±1493.17 (P=0.001); GAIS improvement 88.9% versus 5.9% (P<0.001)	AEs 5.8% versus 9.6%; no serious AEs; wrinkle score and dermal thickness not significantly different
Hauser, 1982 [27]	Female hair loss, including postpartum alopecia; historical clinical series; n=65	Placental extract injections; injection route NR	Product, concentration, exact volume, frequency, and cumulative dose NR	NR	Overall improvement in 74% and complete recovery in 43%; reported; subgroup postpartum subgroup: denominators and improvement in 91% response criteria and complete recovery unavailable; in 64%	No controlled comparison and subgroup criteria adverse events not

described in the abstract;
spontaneous postpartum hair recovery cannot be excluded

Abbreviations: AE, adverse event; EQ-5D-5L, EuroQol 5-Dimension 5-Level; GAIS, Global Aesthetic Improvement Scale; HPE, human placental extract; HPH, human placental hydrolysate; NR, not reported; PPI, placental polypeptide injection; RCT, randomized controlled trial; SC, subcutaneous; SPADI, Shoulder Pain and Disability Index; TMD, temporomandibular disorder; VAS, visual analog scale.

Table 3. Parenteral human placental extract in oral submucous fibrosis

Study	Design / N	Placental intervention route	Frequency and Duration Follow-up	/ / Comparator	Main efficacy findings	Safety Interpretation
Goyal et al., 2024 [18]	Randomized controlled trial; n=160; 40/group	Placentrex 2 mL + 1 mL 2% lignocaine; intralesional	Weekly × 12 weeks; follow-up to 12 months	Supplements/exercises; hyaluronidase+dexamethasone; combination regimen	Week-12 mouth-opening gains: Placentrex 5.94±0.84 mm; combination 7.30±0.80 mm; steroid/hyaluronidase 5.11±0.92 mm; control 0.37±0.16 mm. Relapse: Placentrex 1.62±0.45 mm; combination 0.20±0.08 mm	Combination treatment produced greater and more durable improvement
Kisave et al., 2020 [19]	Comparative clinical study; n=60	Placentrex; intraoral/submucosal injection	Repeated treatment over approximately 2 months; exact injection schedule pending full-text extraction	Hydrocortisone-based treatment	Both approaches improved clinical manifestations; hydrocortisone produced greater improvement in selected outcomes	Comparative evidence; exact group-specific numerical results require confirmation
Ek et al., 2023 [20]	Prospective comparative study; 35 enrolled, 30 completed	Placentrex 2 mL; 35 intralesional injection into fibrotic bands	Weekly × 6 weeks; treatment-period assessment	Dexamethasone mg hyaluronidase 1,500 IU	Mouth-opening improvement 4.3±0.57 mm with Placentrex + versus 7.2±0.76 mm with comparator; burning reduction 1.2±0.73 versus 3.6±0.63; between-group differences P<0.001	Both treatments improved with symptoms; burning numerical results favored comparator
Zuali et al., 2023 [21]	Prospective randomized intervention study; n=58; 29/group	Purified HPE 1 mL; intralesional/submucosal buccal mucosa and retromolar trigone	Weekly × 5 weeks; follow-up to 5 months	Fibrotomy + topical placental extract gel	Mouth-opening improvement 3.14 mm in injection group versus 5.00 mm after fibrotomy; P<0.001 for between-group difference. Absence of burning at 5 months: 44.8% versus 31.0%; between-group difference NS	Fibrotomy produced greater improvement in mouth opening; interventions differ substantially

Naik et al., 2012 [26]	Comparative study with random allocation; n=60; 30/group	Placentrex 2 mL intralesionally/submucosally	Weekly × 8 weeks; eight planned injections; 16 mL total; no additional post-treatment follow-up	Triamcinolone acetonide 10 mg/mL hyaluronidase 1,500 IU	Mouth opening increased from 15.83 to 33.80 mm with Placentrex versus 16.27 to 35.90 mm with comparator. Between-group difference at week 8: 2.10 mm (95% CI 1.20–3.00; P<0.001). Burning P=0.167; mucosal appearance P=0.960	No injection-related complications reported; comparator produced greater final mouth opening
Reddy et al., 2022*	Comparative clinical study; n=30	Placentrex; intraoral submucosal injection	Repeated injections; exact regimen and follow-up pending full-text verification	Corticosteroid injections	Both approaches showed clinical improvement; differences were not consistently statistically significant	Additional comparative evidence; full numerical extraction pending

Reddy et al. is retained as a supplementary study pending complete verification of the original report and its bibliographic placement in the final reference list.

Abbreviations: HPE, human placental extract; NR, not reported; NS, not statistically significant; OSMF, oral submucous fibrosis.

Table 4. Summary of clinical evidence according to indication, route, dosing pattern, and evidence gaps

Clinical domain	Predominant route	Regimens investigated	Principal findings	efficacy	Follow-up Durability	Major limitations
Healthy aging / physical function	SC	Step-down regimen, 2–4 mL; 32 mL over 8 weeks	Significant group improvement in physical (P=0.036)	between- function	Eight-week prolonged follow-up	Small sample; no frailty, mortality, biological-age, or lifespan endpoints
Menopausal symptoms	SC / pharmacopuncture	Commonly 2 mL; 2–3 times weekly; and protocols approximately 2–9 weeks	Improvement in KMI and several menopausal symptom measures in selected trials; negative primary hot-flash trial		Mostly short-term	Heterogeneous preparations; substantial placebo response; inconsistent findings
Chronic fatigue	SC	Three times weekly × 6 weeks	Significant FSS, VAS, and MFI improvements in CFS subgroup	Primarily end-of-treatment assessment		Subgroup effect; subjective endpoints; limited post-treatment follow-up
ASH/NASH / liver disease	IM or SC	Laennec 4 mL IM twice weekly × 24 weeks in pilot; more intensive regimens in comparative trial	Biochemical improvement; non-inferiority reported for ALT endpoint; exploratory histological signal		Up to 24 weeks	ALT is a surrogate endpoint; small biopsy sample; no established fibrosis or long-term clinical-outcome benefit
Shoulder impingement	Targeted subacromial injection	4 mL weekly × 3	Significant improvements in VAS, SPADI, and EQ-5D-5L		Nine weeks after final injection	Single relatively small RCT; requires replication
Temporomandibular disorder	Pharmacopuncture	Ten sessions over five weeks	Pain and functional improvement in selected outcomes		Up to week 25	Active comparator; technique limits extrapolation
OSMF	Intralesional submucosal	Usually 1–2 mL/session; repeated weekly treatment over 5–12 weeks	Improvements in mouth opening and burning; active comparators or		Up to 12 months	Heterogeneous adjunctive treatments; variable relapse;

				combination treatments superior in some studies	inconsistent outcome reporting
Sensitive skin / aesthetic dermatology	Intradermal mesotherapy	4 mL/session × 3		Reduced facial Day 90; hemoglobin content; approximately GAIS response 88.9% 30 days after versus 5.9% final treatment	Open-label; no- treatment comparator; several objective secondary outcomes NS
Female alopecia	NR	NR		Historical series of 65 women: 74% overall improvement and 43% complete recovery; NR postpartum subgroup: 91% improvement and 64% complete recovery	Uncontrolled historical study; spontaneous recovery possible; insufficient protocol and safety information
Longevity	—	No regimen	established	No demonstrated lifespan extension or — mortality reduction	Existing studies assess symptoms, function, or surrogate outcomes rather than longevity

General note for Tables 1–4: Different human placental preparations should not be considered dose-equivalent on the basis of injection volume alone. Manufacturing processes, extraction or hydrolysis methods, concentration, molecular composition, excipients, and regulatory specifications differ among products. The regimens presented in these tables describe the interventions investigated in the original studies and should not be interpreted as clinical dosing recommendations.