

Platelet-rich plasma as an *in vitro* supplement to human sperm cryopreservation and preparation media: A systematic review

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Abstract. Male infertility affects an estimated 9-15% of the male population, and both cryopreservation and laboratory sperm preparation can impair sperm function. Platelet-rich plasma (PRP), a concentrate of platelet-derived growth factors, has been proposed as a supplement to sperm-handling media. The present systematic review evaluated whether the *in vitro* supplementation of human sperm cryopreservation or preparation media with PRP improves sperm quality. For this purpose, the PubMed, the Cochrane Library, ScienceDirect and Google Scholar databases were searched, supplemented by manual searching, for articles published between 2019 and December, 2025. Original studies that added PRP or plasma rich in growth factors to human semen or spermatozoa *in vitro* and compared the results with an untreated or alternative-medium control were eligible. Animal studies and studies using *in vivo* PRP administration were excluded. Risk of bias was assessed with the RoB 2 tool, and the findings were synthesized narratively. Of the 234 records identified, 155 were removed before screening and 30 were excluded on title or abstract screening. Of the 27 full-text reports assessed, 14 studies (532 human semen samples) were included: Seven on cryopreservation and seven on fresh sperm preparation or incubation. The overall risk of bias was low in four studies, raised some concerns in nine and was high in one study. PRP was associated with higher post-thaw or post-preparation motility in the majority of studies and with improved viability, DNA fragmentation and oxidative stress markers in several studies. However, the effects were inconsistent, lower concentrations generally outperformed higher ones, and PRP used alone as a cryoprotectant was detrimental. A meta-analysis was not performed owing to heterogeneity, and no study reported clinical reproductive

or safety outcomes. In summary, limited *in vitro* evidence suggests that low-concentration PRP, used as a supplement to standard media, may improve laboratory measures of human sperm quality. Its clinical benefit and safety remain unproven, and standardized PRP preparation and adequately powered studies with reproductive outcomes are required.

Introduction

Male infertility is a global health concern that contributes to ~30% of infertility cases and affects an estimated 9-15% of the male population. Its burden increased by 76.9% between 1990 and 2019. Beyond its reproductive consequences, male infertility is associated with anxiety, depression, stigma and marital stress, and with a higher risk of cancer and a reduced life expectancy (1-3).

Platelet-rich plasma (PRP) is an autologous blood product in which platelets are concentrated above baseline levels. Upon activation, platelets release growth factors, including platelet-derived growth factor, transforming growth factor- β , vascular endothelial growth factor, insulin-like growth factor-I (IGF-I) and fibroblast growth factor (FGF), together with cytokines and plasma proteins (4-6). The composition of PRP varies considerably with the preparation method, particularly in its platelet and leukocyte content (7). In male reproduction, PRP has been investigated in three distinct settings: Intratesticular injection in men with non-obstructive azoospermia or severe oligoasthenoteratozoospermia (8,9), the culture of spermatogonial stem cells (10) and the *in vitro* supplementation of media used to cryopreserve or prepare ejaculated spermatozoa (5,11). These settings differ in their target cells, plausible mechanisms, evidence base and clinical implications, and should therefore be evaluated separately.

The present systematic review focused on the *in vitro* setting. Cryopreservation exposes spermatozoa to cold shock, osmotic stress, ice crystal formation and oxidative stress, and laboratory preparation by centrifugation, filtration or swim-up can also generate reactive oxygen species (ROS). These insults reduce motility and viability and damage sperm DNA (5,12). As mature spermatozoa have limited capacity for repair, protective supplements in the surrounding medium have been explored, and PRP has attracted interest as an inexpensive, autologous source of growth factors and antioxidant plasma

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components (11). Previous narrative reviews have combined *in vitro*, intratesticular and animal data (5,9,11), and the human *in vitro* evidence has not been systematically appraised.

The present systematic review therefore aimed to determine whether the *in vitro* supplementation of human sperm cryopreservation or preparation media with PRP improves sperm quality compared with no PRP or an alternative medium, to assess the risk of bias of the available studies, and to summarize the evidence on PRP concentration, possible mechanisms and safety.

Data and methods

Protocol and reporting. The present systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement (13). The review protocol was prospectively registered in PROSPERO (CRD420261481413).

Eligibility criteria. The eligibility criteria were defined using the population, intervention, comparator, outcome and study design framework. The population comprised ejaculated human semen samples or spermatozoa from fertile, normozoospermic or infertile men. The intervention was the *in vitro* addition of PRP or plasma rich in growth factors (PRGF), whether autologous or heterologous and at any concentration, to semen, cryopreservation medium or sperm preparation or incubation medium. The comparator was the same or comparable samples processed without PRP or with an alternative medium or supplement. The primary outcome was progressive or total sperm motility. Secondary outcomes were viability, morphology, membrane integrity, DNA fragmentation, oxidative stress markers and any reported adverse effect. Eligible designs were original controlled laboratory experiments, including split-sample designs, and randomized or non-randomized comparative studies, published in English as full-text peer-reviewed articles. Animal studies, studies with *in vivo* PRP administration, studies on non-sperm cells, reviews, systematic reviews, meta-analyses, letters, notes, case reports, case series and conference abstracts without a full text were excluded.

Information sources and search strategy. The PubMed, the Cochrane Library, ScienceDirect and Google Scholar databases were searched for articles published from January, 2019 to December, 2025, and manual searching of the reference lists of relevant articles was also performed. The search terms 'platelet rich plasma' OR 'PRP' were combined using AND with 'sperm quality', 'sperm retrieval media' and 'infertility', in various combinations, in the title and abstract fields. The search was restricted to English-language publications.

Study selection. Following the removal of duplicates, the two authors (JCS and RP) independently screened the titles and abstracts and then assessed the full texts of potentially eligible reports against the eligibility criteria. Disagreements were resolved by discussion.

Data extraction. Data were extracted using a standardized form that recorded the first author, year of publication,

country, study design, application setting (cryopreservation or fresh preparation/incubation), number and characteristics of semen samples, age of donors, PRP source and concentration, comparator, outcome data and main conclusions. Data were extracted by one author and verified by the second.

Risk of bias assessment. Risk of bias was assessed independently by two reviewers using the revised Cochrane risk-of-bias tool for randomized trials (RoB 2) (14). The tool covers five domains: Bias arising from the randomization process (D1), bias due to deviations from intended interventions (D2), bias due to missing outcome data (D3), bias in measurement of the outcome (D4) and bias in selection of the reported result (D5). Each domain and each study overall was rated as low risk, some concerns or high risk. As the majority of the included studies were laboratory experiments in which aliquots of the same sample were allocated to the experimental arms, D1 was applied to the allocation of samples or aliquots to treatment arms, and D2 to adherence to the stated laboratory protocol. Disagreements were resolved by consensus, and the results were visualized using robvis (15).

Synthesis methods. A meta-analysis was not performed due to substantial clinical and methodological heterogeneity. The included studies differed in PRP source (autologous or heterologous), preparation and activation, concentration (expressed variously as % v/v, platelets/ μ l or an absolute volume), application setting, sperm population, outcome definitions and timing of assessment, and several did not report the measures of variance required for pooling. The findings were therefore synthesized narratively in accordance with the Synthesis Without Meta-analysis (SWiM) guideline (16). Studies were grouped by application setting, and the direction of effect was summarized for each outcome. Studies were not weighted, and the result of the study at high risk of bias was interpreted with caution.

Results

Study selection. The search identified 234 records (PubMed, n=78; Google Scholar, n=31; Cochrane Library, n=24; ScienceDirect, n=82; manual search, n=19). Before screening, 62 duplicates, 52 records outside the publication period and 41 records for other reasons were removed, leaving 79 records for title and abstract screening. Of these, 30 were excluded (21 on title and 9 on abstract). Of the 49 reports sought for retrieval, 22 could not be retrieved in full text, and 27 were assessed for eligibility. A total of 13 reports were excluded (12 reviews, systematic reviews or meta-analyses and 1 study of intratesticular PRP injection), and 14 studies were included (Fig. 1).

Characteristics of the included studies. The characteristics and findings of the 14 included studies are summarized in Table I. The studies were published between 2020 and 2025 and were conducted in Iran (n=6), Iraq (n=3), China, Indonesia, Lebanon, Turkey and Thailand (n=1 each). They analyzed a total of 532 human semen samples (range, 10-100 per study). Of note, one study was a pilot randomized controlled trial (17), one was a prospective paired comparative study (18) and 12 were controlled *in vitro* laboratory experiments, in most of which aliquots of the same sample served as the control. A

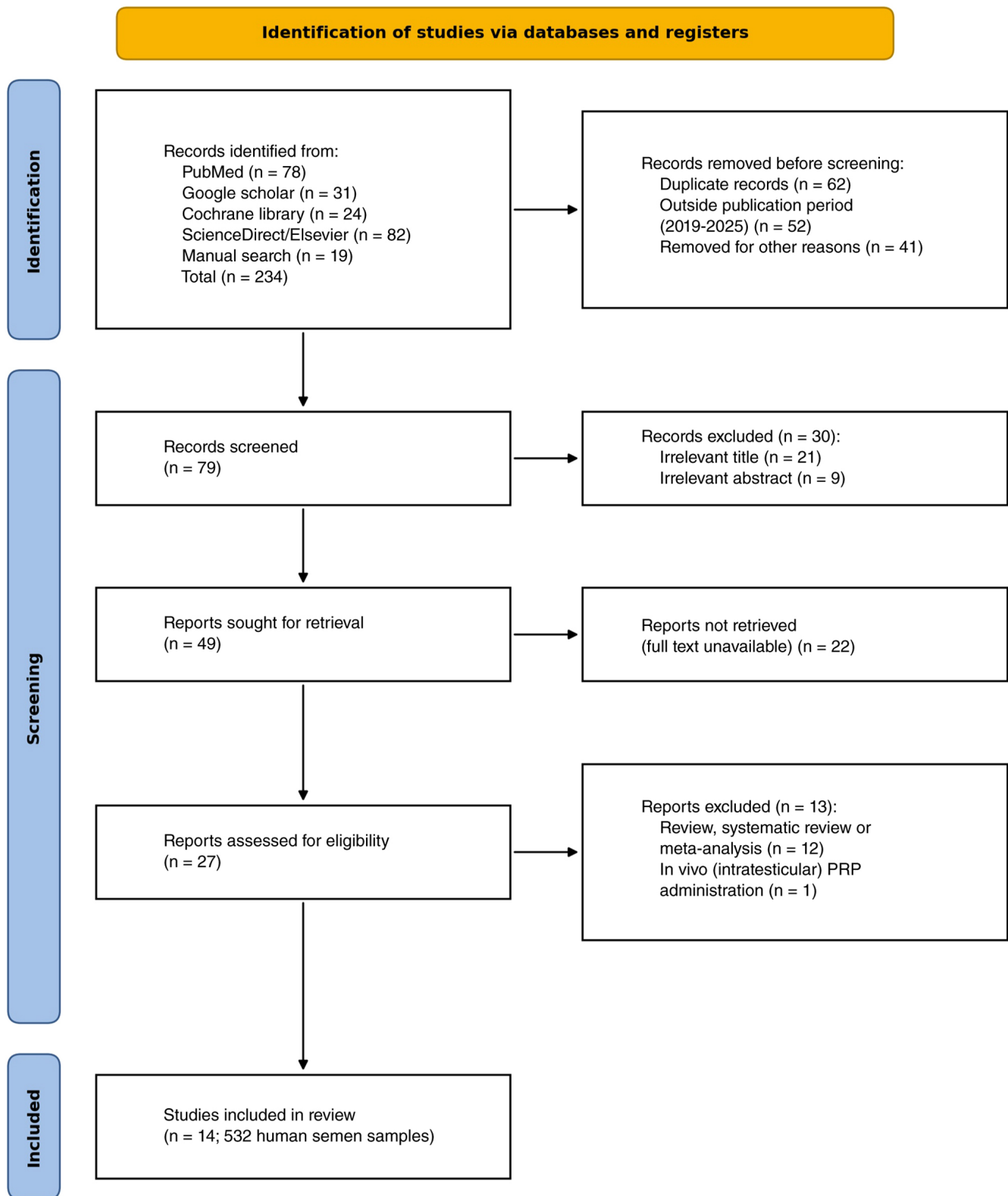


Figure 1. PRISMA 2020 flow diagram of the study selection process.

total of seven studies (157 samples) evaluated PRP as a supplement during cryopreservation (12,18-23) and seven studies (375 samples) evaluated PRP during fresh sperm preparation or incubation, including glass wool filtration, swim-up and incubation under oxidative stress (17,24-29). The samples were derived from normozoospermic donors and from men

with infertility, asthenoteratozoospermia, teratozoospermia or oligoasthenoteratozoospermia. PRP was autologous in the majority of the studies, heterologous or non-autologous in two studies (23,29) and prepared as PRGF in two studies (19,28). Concentrations ranged from 0.25 to 10% v/v, from 50×10^3 to 100×10^3 platelets/ μ l, or 0.5 ml of undiluted PRP.

Table I. Characteristics and findings of the included studies, grouped by application setting.

A, PRP as a supplement during cryopreservation (7 studies; 157 samples)											
Authors, year of publication	Country	Design	Samples (n)	Age (years)	PRP type and concentration	Progressive motility (%)	Viability (%)	Total abnormalities (%)	Membrane integrity (%)	Main conclusion	Overall RoB (Refs.)
Yan <i>et al</i> , 2021	China	<i>In vitro</i> experimental	12 semen samples	-	Autologous PRP 2, 5 and 10%	0%: 28.1±2.6 5%: 30.3±2.7 10%: 29.2±2.2	0%: 59.6±3.9 2%: 62.0±3.9 5%: 65.5±4.2 10%: 64.3±3.2	-	0%: 49.2±3.4 2%: 49.8±3.1 5%: 52.4±3.6 10%: 51.5±3.3	PRP increased post-thaw motility and viability and protected spermatozoa from freezing damage and excessive ROS generation; being self-derived, it is an attractive cryoprotective additive.	Low (12)
Mirzaei <i>et al</i> , 2022	Iran	<i>In vitro</i> experimental	10 semen samples	-	PRGF 1, 5 and 10%	0%: 35.4±6.2 1%: 49.0±5.8 5%: 37.1±17.6 10%: 36.0±9.8	0%: 57.8±7.3 1%: 67.3±7.1 5%: 58.0±11.9 10%: 59.6±7.8	-	-	Adding 1% PRGF to freezing medium improved motility, vitality, normal morphology, acrosome integrity, chromatin integrity and DNA fragmentation.	Low (19)
Nabavinia <i>et al</i> , 2023	Iran	<i>In vitro</i> experimental	20 samples	20-30 semen	PRP 0.25, 0.5 and 1x10 ⁵ platelets/ μ l	Control: 20 0.25; 28 0.5; 25 1: 35	Control: 59 0.25: 60 0.5; 60 1: 67	Control: 45 0.25; 47 0.5; 50 1: 53	-	Samples treated with PRP at 1x10 ⁵ platelets/ μ l had significantly higher progressive motility and viability than controls.	Some concerns (20)
Lorian <i>et al</i> , 2024	Iran	<i>In vitro</i> experimental	20 semen samples (OAT)	20-40	Autologous PRP 0.25, 0.5 and 1x10 ⁵ platelets/ μ l	Control: 15.25±1.51 0.25: 12.15±9.65 0.5: 12.35±4.90 1: 14.05±4.13	-	-	-	PRP as a cryoprotectant at all three doses, particularly 1x10 ⁵ platelets/ μ l, may reduce the negative consequences of cryopreservation.	Some concerns (21)
Kamal <i>et al</i> , 2024	Iraq	<i>In vitro</i> experimental	60 semen samples	25-40	Autologous PRP 0.5 ml alone or with 0.7 ml glycerol-sugar medium	Control: 64.85±1.91 PRP alone: 27.22±2.54 PRP + medium: 69.75±2.60	-	-	-	Autologous PRP alone as the cryoprotective agent gave negative results; PRP combined with glycerol-sugar medium gave better semen parameters.	Some concerns (22)

Table I. Continued.

A, PRP as a supplement during cryopreservation (7 studies; 157 samples)											
Authors, year of publication	Country	Design	Samples (n)	Age (years)	PRP type and concentration	Progressive motility (%)	Viability (%)	Total abnormalities (%)	Membrane integrity (%)	Main conclusion	Overall RoB (Refs.)
Soltani <i>et al.</i> , 2025	Iran	<i>In vitro</i> experimental (lab trial)	20 semen samples (asthenoterato zoospermic)	20-40	Heterologous PRP 50x10 ³ and 100x10 ³ platelets/ μ l	Control: 4.27 $\pm$ 0.78 PRP50: 10.65 $\pm$ 1.47 PRP100: 6.96 $\pm$ 0.96	Control: 7.51 $\pm$ 0.60 PRP50: 22.86 $\pm$ 1.68 PRP100: 14.54 $\pm$ 1.24	Control: 0.62 $\pm$ 0.16 PRP50: 0.79 $\pm$ 0.18 PRP100: 0.83 $\pm$ 0.17	-	PRP and nanocurcumin improved motility, viability, DNA fragmentation and oxidative stress markers; PRP at the lower concentration was most effective. Neither improved morphology. 5% autologous PRP significantly improved post-thaw vitality, with no significant effect on concentration, motility, morphology or DNA fragmentation.	Some concerns (23)
Thitipatlerdech <i>et al.</i> , 2025	Thailand	Prospective comparative (paired)	15 paired semen samples (normozoospermic)	27.3 $\pm$ 3.8 (mean)	Autologous PRP 5%	Without vs. with PRP: 5.67 (IQR 8.66) vs. 6.61 (IQR 6.35); P=0.887	26.07 $\pm$ 9.30 vs. 32.13 $\pm$ 12.02; P=0.009	4.40 $\pm$ 1.18 vs. 4.40 $\pm$ 0.98; P>0.999	-		Some concerns (18)
B, PRP during fresh sperm preparation or incubation (7 studies; 375 samples)											
Authors, year of publication	Country	Design	Samples (n)	Age (years)	PRP type and concentration	Progressive motility (%)	Viability (%)	Total abnormalities (%)	Membrane integrity (%)	Main conclusion	Overall RoB (Refs.)
Abduljabar <i>et al.</i> , 2021	Iraq	<i>In vitro</i> experimental (glass wool filtration)	60 semen samples (infertile men)	-	GWF alone vs. GWF + PRP	GWF: 70.72 $\pm$ 11.43 GWF + PRP: 89.62 $\pm$ 4.18	-	-	-	PRP combined with GWF increased progressive motility and reduced immotile spermatozoa compared with GWF alone.	Low (24)
Hamdan <i>et al.</i> , 2021	Iraq	<i>In vitro</i> experimental (incubation)	100 semen samples	-	Autologous PRP 2%	Control: 28.17 $\pm$ 17.31 2%: 39.22 $\pm$ 20.26	-	-	-	Autologous PRP increased the motility of human spermatozoa.	High (25)

Table I. Continued.

B, PRP during fresh sperm preparation or incubation (7 studies; 375 samples)											
Authors, year of publication	Country	Design	Samples (n)	Age (years)	PRP type and concentration	Progressive motility (%)	Viability (%)	Total abnormalities (%)	Membrane integrity (%)	Main conclusion	Overall RoB (Refs.)
Angellee <i>et al.</i> , 2021	Indonesia	<i>In vitro</i> experimental (1-h incubation)	40 semen samples (infertile men)	-	PRP (concentration not reported)	Fresh: 0.30±0.65 PRP: 23.92±14.75	-	-	-	Incubation with PRP for 1 h improved concentration, motility, progressive motility, morphology and the proportion of spermatozoa with good fertilization capacity compared with fresh semen.	Some concerns (26)
Bader <i>et al.</i> , 2020	Lebanon	<i>In vitro</i> experimental (H ₂ O ₂ -induced oxidative stress)	30 semen samples	-	Autologous PRP 2, 5 and 10%	Control: 50 2%; 50 5%; 50 10%; 35	-	Control: 25 2%; 19 5%; 20 10%; 22	-	2% PRP increased progressive and total motility of stressed and non-stressed spermatozoa and decreased ROS-positive cells, DNA fragmentation, vacuolization and dead cells.	Some concerns (27)
Ghasemian Nafchi <i>et al.</i> , 2023	Iran	<i>In vitro</i> experimental (incubation)	25 semen samples (teratozoospermic)	-	PRGF 1, 5 and 10%	Control: 17.36±8.50 1%: 47.72±13.76 5%; 38.54±16.80 72.35±8.41 10%: 38.45±15.87	Control: 71.37±13.29 1%: 81.36±9.65 5%; 9.65 5%;	-	-	PRGF incubation improved sperm parameters and reduced malondialdehyde, a marker of oxidative stress.	Some concerns (28)
Yentur <i>et al.</i> , 2025	Turkey	Pilot randomized controlled trial (swim-up)	40 semen samples	20-45	Autologous non-activated PRP, 0.5 ml undiluted	Total motility, PRP vs. control: 1 h: 97.25±4.92 vs. 93.87±9.96 (P<0.05) 24 h: 50.50±9.79 vs. 21.12±10.03 (P<0.001)	-	-	-	PRP added during swim-up preparation enhanced and preserved motility over 24 h, supporting its potential as an adjunct in IUI/IVF sperm preparation.	Low (17)

Table I. Continued.

B, PRP during fresh sperm preparation or incubation (7 studies; 375 samples)										
Authors, year of publication	Country	Design	Samples (n)	Age (years)	PRP type and concentration	Progressive motility (%)	Viability (%)	Total abnormalities (%)	Membrane integrity (%)	Overall RoB (Refs.)
Hosseini <i>et al</i> , 2025	Iran	<i>In vitro</i> experimental, split-sample (incubation and swim-up)	80 semen samples (40 normozoospermic, 40 asthenoteratozoospermic)	20-45	Non-autologous PRP 2%	Asthenoteratozoospermic, control vs. PRP: Incubation: 15.4±7.7 vs. 22.4±4.2 Swim-up: 52.6±5.6 vs. 59.5±3.4 (both P<0.001)	59.2±8.7 vs. 61.6±6.6; P=0.172	No significant change	-	2% PRP improved motility (and concentration after swim-up) in normozoospermic and asthenoteratozoospermic samples, with no significant effect on viability or morphology.

Values are presented as reported in the original studies (mean ± SD unless otherwise indicated); -, not reported. Concentrations are % v/v unless otherwise stated. Overall RoB was assessed with the RoB 2 tool (Fig. 2). PRP, platelet-rich plasma; PKGF, plasma rich in growth factors; OAT, oligoasthenoteratozoospermia; GWF, glass wool filtration; ROS, reactive oxygen species; IQR, interquartile range; IUI, intrauterine insemination; IVF, *in vitro* fertilization; RoB, risk of bias.

Risk of bias. The risk of bias assessment is presented in Fig. 2. The overall risk of bias was low in four studies (12,17,19,24), raised some concerns in nine and was high in one study (25). All studies were at low risk of bias in D1. The most frequent concerns related to missing outcome data (D3; five studies), deviations from intended interventions (D2; four studies) and measurement of the outcome (D4; four studies, including the study at high risk of bias). Only one study raised concerns about selective reporting (D5) (20). Sample sizes were small (median, 27.5 samples per study).

Effect of PRP during cryopreservation. Of the seven cryopreservation studies, five reported an improvement in at least one motility or viability outcome with PRP as a supplement. Yan *et al* (12) reported modestly higher post-thaw progressive motility (30.3 vs. 28.1%), viability (65.5 vs. 59.6%) and membrane integrity with 5% autologous PRP, together with lower ROS generation. Mirzaei *et al* (19) reported that 1% PRGF improved progressive motility (49.0 vs. 35.4%), viability (67.3 vs. 57.8%), morphology, acrosome and chromatin integrity and DNA fragmentation, whereas 5 and 10% were less effective. Nabavinia *et al* (20) found the greatest improvements in progressive motility (35 vs. 20%) and viability (67 vs. 59%) with 1x10⁵ platelets/μl. Soltani *et al* (23) reported that heterologous PRP at 50x10³ platelets/μl improved progressive motility (10.65 vs. 4.27%) and viability (22.86 vs. 7.51%) and reduced DNA fragmentation and malondialdehyde (MDA) levels in samples from men with asthenoteratozoospermia, and was more effective than 100x10³ platelets/μl and nanocurcumin, although morphology did not improve.

The remaining findings were less favorable. Thitipatlerdech *et al* (18) found that 5% autologous PRP improved post-thaw vitality in normozoospermic men (32.13 vs. 26.07%; P=0.009) but not progressive motility, morphology or DNA fragmentation. Lorian *et al* (21) concluded that PRP exerted a cryoprotective effect in oligoasthenoteratozoospermic samples, particularly at 1x10⁵ platelets/μl, although the extracted progressive motility values did not exceed those of the control (14.05 vs. 15.25%). Kamal *et al* (22) reported that 0.5 ml of autologous PRP used alone as the cryoprotective agent markedly reduced post-thaw progressive motility (27.22 vs. 64.85%), whereas PRP combined with a glycerol-sugar cryoprotective medium produced a small improvement (69.75%). This indicates that PRP cannot replace a conventional penetrating cryoprotectant.

Effect of PRP during fresh sperm preparation or incubation. All seven studies in this setting reported higher motility with PRP. Abduljabar *et al* (24) reported higher progressive motility after glass wool filtration combined with PRP than after filtration alone (89.62 vs. 70.72%). Hamdan *et al* (25) reported higher progressive motility after incubation with 2% autologous PRP (39.22 vs. 28.17%), although this study was at high risk of bias. Angellee *et al* (26) reported that 1 h of incubation with PRP improved concentration, motility, progressive motility, morphology and the proportion of spermatozoa with good fertilization capacity in men undergoing infertility treatment. Under H₂O₂-induced oxidative stress, Bader *et al* (27) found that 2% PRP increased progressive

		Risk of bias domains					
		D1	D2	D3	D4	D5	Overall
Study	Yan et al (12)						
	Mirzaei et al (19)						
	Nabavinia et al (20)						
	Abduljabar et al (24)						
	Hamdan et al (25)						
	Angellee et al (26)						
	Lorian et al (21)						
	Kamal et al (22)						
	Bader et al (27)						
	Ghasemian Nafchi et al (28)						
	Soltani et al (23)						
	Yentur et al (17)						
	Thitipatlertdech et al (18)						
	Hosseini et al (29)						

Domains:

D1: Bias arising from the randomization process.

D2: Bias due to deviations from intended interventions.

D3: Bias due to missing outcome data.

D4: Bias in measurement of the outcome.

D5: Bias in selection of the reported result.

Judgement

High

Some concerns

Low

Figure 2. Risk of bias of the included studies assessed using the RoB 2 tool. D1, bias arising from the randomization process; D2, bias due to deviations from intended interventions; D3, bias due to missing outcome data; D4, bias in measurement of the outcome; D5, bias in selection of the reported result. Green, low risk; yellow, some concerns; red, high risk.

and total motility and reduced ROS-positive cells, DNA fragmentation, vacuolization and dead cells, whereas 10% PRP reduced progressive motility below control levels (35 vs. 50%). In teratozoospermic samples, Ghasemian Nafchi *et al* (28) reported that 1% PRGF improved progressive motility (47.72 vs. 17.36%) and viability (81.36 vs. 71.37%) and reduced MDA, while higher concentrations were less effective. In a pilot randomized controlled trial, Yentur *et al* (17) found that non-activated autologous PRP added during swim-up preserved total motility over 24 h (50.50 vs. 21.12%; $P < 0.001$). Hosseini *et al* (29) reported that 2% non-autologous PRP improved progressive motility after incubation and after swim-up in asthenoteratozoospermic samples, with no effect on viability or morphology.

Concentration. In total, seven studies compared two or more PRP concentrations. The best-performing arm was the lowest concentration tested in four studies (19,23,27,28), an intermediate concentration in one (12) and the highest in two, both of which tested only a narrow, low range of up to 1×10^5 platelets/ μ l (20,21). The highest concentrations tested (10% v/v or 100×10^3 platelets/ μ l) were never the most effective, and in one study they were detrimental (27). As the concentrations were expressed in incompatible units, a common optimal dose could not be derived.

Clinical and safety outcomes. None of the included studies reported fertilization, embryo development, pregnancy, live birth or offspring outcomes, and none systematically reported adverse effects.

Discussion

The present systematic review identified 14 *in vitro* studies, comprising 532 human semen samples, that evaluated PRP as a supplement to sperm cryopreservation or preparation media. Most studies reported higher motility with PRP, and several reported improved viability, DNA fragmentation and oxidative stress markers. However, the benefit during cryopreservation was inconsistent, the effect appeared to depend on concentration, and PRP was detrimental when used alone as a cryoprotectant. The evidence consists of small laboratory studies with surrogate outcomes, most of which raised some concerns about risk of bias, and no study assessed clinical reproductive outcomes or safety. These findings therefore support further investigation, but not clinical use, of PRP-supplemented sperm media.

Quality and external validity of the evidence. Several features limit the strength of the evidence. First, sample sizes were small (10-100 samples) and most studies were single laboratory experiments; small, positive studies are also more likely to be published. Second, although split-sample designs control for between-donor variability, manual semen analysis is susceptible to observer bias when assessors are aware of the allocation, which is reflected in the concerns in D4. Third, RoB 2 was developed for randomized clinical trials, and its application to laboratory experiments required interpretation of D1 and D2, so the ratings should be regarded as approximate. Fourth, the outcomes were laboratory surrogates, and improvements of a few percentage points in post-thaw motility [for example, 30.3 vs. 28.1% (12)] may not be biologically or clinically meaningful. Finally, six of the 14 studies were conducted in Iran and three in Iraq, which may limit generalizability.

Studies on buck (30), ram (31,32) and buffalo bull (33,34) semen have also reported improved post-thaw quality with PRP-supplemented extenders, and some reported *in vivo* fertility. However, species differences in sperm membrane composition, cryotolerance, extenders and the preparation of PRP mean that these data cannot be extrapolated to human male infertility.

Concentration and formulation. The most consistent pattern was non-linear: Low to moderate concentrations (1-5% v/v or 50×10^3 - 1×10^5 platelets/ μ l) generally exhibited optimal performance, whereas the highest concentrations tested were never superior and occasionally harmful (19,23,27,28). One explanation is that the beneficial growth factors and antioxidants of PRP are accompanied by components that are harmful at higher doses, including leukocyte-derived ROS and pro-inflammatory cytokines, and fibrinogen and other clotting factors that may cause sperm agglutination or entrapment (7,35). Agglutination at higher PRP concentrations has been reported in animal semen (30,31,34), although not systematically assessed in the human studies. The finding of the study by Kamal *et al* (22) that PRP alone is detrimental, whereas PRP with a conventional cryoprotectant is beneficial further suggests that PRP acts as an adjunct and not as a cryoprotectant in its own right. Interpretation across studies is limited because PRP source, platelet and leukocyte content,

anticoagulant and activation method were not consistently reported, and because concentrations were expressed as % v/v, platelets/ μ l or absolute volume. Standardized reporting, preferably of the final platelet and leukocyte concentration in the medium, is required.

Mechanisms. Mature spermatozoa are transcriptionally and translationally largely inactive. Any short-term *in vitro* effect of PRP must therefore arise from direct interactions with the extracellular medium or from rapid, non-genomic signaling, and not from changes in gene expression. This distinction is critical when mechanisms are inferred from other cell types.

The best-supported mechanism is a reduction in oxidative stress. Human sperm membranes are rich in polyunsaturated fatty acids and the cells have limited cytoplasmic antioxidant capacity, rendering them vulnerable to lipid peroxidation, loss of motility and DNA damage during cryopreservation and handling. Notably, four included studies directly measured oxidative stress and reported lower ROS generation (12), fewer ROS-positive cells under H_2O_2 challenge (27) or lower MDA levels (23,28) with PRP. Plasma antioxidant proteins and enzymes in PRP may scavenge ROS in the medium. In tenocytes, PRP increases antioxidant defenses through the Nrf2 signaling pathway (36); however, as this pathway depends on transcription, it is unlikely to operate in mature spermatozoa, and direct scavenging and membrane protection are more plausible in this setting.

A second mechanism involves growth factor receptor signaling. Human spermatozoa express functional FGF receptors in the acrosomal region and flagellum, and FGF2 increases sperm motility through receptor tyrosine kinase activation (37). Endogenous sperm FGF2 levels are positively associated with motility, and recombinant FGF2 increases the recovery of motile spermatozoa after swim-up (38), which is consistent with the swim-up findings of Yentur *et al* (17) and Hosseini *et al* (29). IGF-I from seminal plasma has been reported to influence capacitation, membrane integrity and DNA fragmentation in goat spermatozoa (39), although this has not been confirmed in human spermatozoa. Plasma proteins may also stabilize sperm membranes against osmotic and cold stress. Importantly, none of the included studies measured the growth factor content of the PRP used, receptor activation or mitochondrial function in relation to the observed effects, so these mechanisms remain inferred rather than demonstrated.

Mechanisms such as the stimulation of Leydig cell function and steroidogenesis, repair of testicular tissue and support of spermatogonial stem cells have been described in animal models of testicular injury (40,41) and in stem cell culture (10). These are relevant only to *in vivo* or intratesticular PRP administration and do not apply to ejaculated spermatozoa exposed to PRP *in vitro*.

Safety. None of the included studies systematically reported adverse effects, and none followed fertilization, embryo development, pregnancy or offspring outcomes, so the safety of PRP-exposed spermatozoa for assisted reproduction is unknown. Several potential risks merit consideration. First, direct sperm toxicity is possible: PRP used alone impaired post-thaw motility (22) and 10% PRP reduced motility under oxidative stress (27), and leukocyte-rich PRP formulations

have shown cytotoxicity in other human cell types (35). Second, sperm agglutination may occur at higher concentrations or after platelet activation and clot formation (30,31,34). Third, the use of heterologous or non-autologous PRP (23,29) carries a risk of transmitting blood-borne pathogens into the laboratory and to the female partner or embryo, and would require donor screening and compliance with tissue and cell regulations; even autologous PRP requires venepuncture and sterile processing to avoid microbial contamination. Fourth, immunological effects are theoretically possible: allogeneic plasma proteins could provoke immune responses, and the autologous plasma of some infertile men may contain antisperm antibodies that could promote agglutination or immobilization. Finally, the local risks of intratesticular injection, such as pain, hematoma, inflammation and infection, were outside the scope of the present systematic review and require separate evaluation. Until these issues have been addressed, PRP-supplemented sperm media should be restricted to research settings.

Comparison with other approaches. Only two included studies compared PRP with another active approach: PRP outperformed glass wool filtration alone (24) and nanocurcumin (23). No study compared PRP with established antioxidant supplements or commercial cryoprotective media, so its relative effectiveness is unknown.

Limitations. The present review has certain limitations which should be mentioned. The search was restricted to English-language articles published between 2019 and 2025; thus, earlier studies were not captured. A total of 22 potentially relevant reports could not be retrieved in full text, which may have introduced selection bias. Some data could only be extracted approximately from the published reports. Finally, meta-analysis was not possible, and the certainty of evidence was not formally graded.

Future research. Future studies are warranted to report PRP preparation in detail, including the source, platelet and leukocyte counts, anticoagulant, activation method and final concentration in the medium. They should use adequately powered, randomized split-sample designs with blinded, computer-assisted semen analysis, together with functional outcomes such as DNA fragmentation, mitochondrial membrane potential and capacitation. Studies should also measure the growth factor and cytokine content of the PRP used. If such studies confirm a reproducible benefit, controlled clinical trials with fertilization, embryo, pregnancy, live birth and safety outcomes will be required before PRP-supplemented media can be recommended in assisted reproduction.

In conclusion, limited *in vitro* evidence from small studies suggests that low-concentration PRP, used as a supplement to standard cryopreservation or preparation media, may improve laboratory measures of human sperm quality, particularly motility. The effect is inconsistent, appears to depend on concentration and is lost or reversed when PRP replaces a conventional cryoprotectant. PRP-supplemented sperm media should therefore be regarded as experimental until standardized protocols and adequately powered studies with clinical and safety outcomes are available.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

JCS conceptualized the study, conducted the literature search, screened the studies, extracted the data, assessed the risk of bias, performed the synthesis and drafted the manuscript. RP contributed to the study design, independently screened the studies, verified the extracted data, assessed risk of bias, interpreted the findings and critically revised the manuscript. JCS and RP confirm the authenticity of all the raw data. Both authors have read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Use of artificial intelligence tools

During the revision of this manuscript, the authors used an artificial intelligence tool (Claude; Anthropic) to assist with restructuring the text in response to the peer review comments and with language editing. The authors reviewed and edited all output and take full responsibility for the content of the manuscript.

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