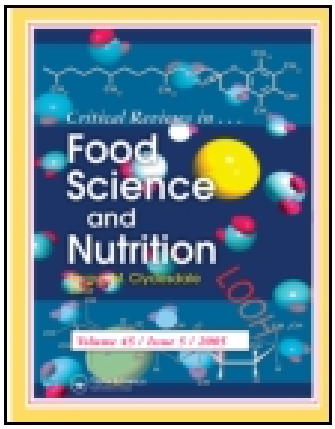

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Pyruvate Supplementation for Weight Loss: A Systematic Review and Meta-Analysis of Randomized Clinical Trials

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Pyruvate Supplementation for Weight Loss: A Systematic Review and Meta-Analysis of Randomized Clinical Trials

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***Background**: Several slimming aids being sold as food supplements are widely available. One of them is pyruvate. Its efficacy in causing weight reduction in humans has not been fully established. The objective of this systematic review was to examine the efficacy of pyruvate in reducing body weight.*
***Methods:** Electronic and nonelectronic searches were conducted to identify all relevant human randomized clinical trials. The bibliographies of all located articles were also searched. No restrictions in language or time were applied. Two independent reviewers extracted the data according to predefined criteria. A fixed-effect model was used to calculate mean differences (MD) and 95% confidence interval (CI).*
***Results:** Nine trials were identified and 6 were included. All had methodological weaknesses. The meta-analysis revealed a statistically significant difference in body weight with pyruvate compared to placebo (MD: −0.72 kg; 95% CI: −1.24 to −0.20). The magnitude of the effect is small, and its clinical relevance is uncertain. Adverse events included gas, bloating, diarrhea, and increase in low-density lipoprotein (LDL) cholesterol.*
***Conclusion:** The evidence from randomized clinical trials does not convincingly show that pyruvate is efficacious in reducing body weight. Limited evidence exists about the safety of pyruvate. Future trials involving the use of this supplement should be more rigorous and better reported.*

Keywords Obesity, body weight, weight loss, meta-analysis

INTRODUCTION

There is growing concern over the increasing numbers of overweight and obese individuals, and management of obesity has become an important component of public health agenda. Several weight-management strategies are now available (Joyal, 2004), and a wide variety of slimming aids usually marketed as food supplements are on offer. The efficacy of these food supplements has not been proven, yet they are sold as over-the-counter preparations, and on the internet. One such slimming aid is pyruvate.

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Pyruvate (a derivative of pyruvic acid) is a breakdown product of normal body metabolism. It is a 3-carbon intermediate product of the glycolysis pathway (Koh-Banerjee et al., 2005). It can be converted to lactate or to acetyl-CoA in the cytoplasm or mitochondria, respectively. Pyruvate is present in cheese, apples, and red wine. Although there is a lack of consensus on its mechanism of action, some authors have suggested that pyruvate induces weight loss via increased metabolism in muscle tissue (Koh-Banerjee et al., 2005). It has also been postulated that pyruvate enhances physical endurance during rest or exercise, by increasing blood glucose extraction from exercising muscle (Stanko et al., 1990).

Pyruvate is sold in the different formulations, with calcium pyruvate being one of the most common ones. Some animal studies have suggested that diet supplementation with pyruvate

causes weight loss (Cortez et al., 1991). However, the efficacy of pyruvate in humans is has not been fully established.

The aim of this systematic review was to summarize and critically evaluate the evidence from randomized clinical trials (RCTs) involving the use of pyruvate as a weight loss supplement.

METHODS

Electronic searches of literature were conducted in the following databases: Medline, Embase, *The Cochrane Library*, Amed, and Cinahl. The search terms used included dietary supplement, nonprescription drug, pyruvic acid, body composition, body mass index, clinical trial, and derivatives of these. Each database was searched from inception until July, 2010. Hand searches of relevant medical journals and of our own files were also conducted. The bibliographies of all located articles were also searched. Where necessary, contact was made with relevant authors to gather relevant details relating to a trial report.

Only randomized, double-blind, placebo-controlled studies were included in this review. To be considered for inclusion, studies had to test the efficacy or effectiveness of oral pyruvic acid or any of its salts for weight reduction in overweight humans. Included studies also had to report body weight or body composition as an outcome. No age restrictions were imposed for inclusion of studies. RCTs were included irrespective of whether or not, they incorporated lifestyle modification into their trial regimen. Studies involving the use of pyruvate as part of a combination product or treatment package were excluded from the systematic review. There were no language restrictions imposed for this review.

Two independent reviewers assessed the eligibility of studies to be included in the review. Data were extracted systematically by 2 independent reviewers according to patient characteristics, interventions, and results. The methodological quality of all included trials was assessed using a quality assessment tool checklist adapted from the Consolidated Standard for the Reporting of Randomized Clinical Trials (CONSORT) guidelines (Moher et al., 2001; Altman et al., 2001). Disagreements were resolved through discussions with the other authors.

Data are presented as means with standard deviations. Mean changes in body weight and body fat mass were used as common endpoints to assess the differences between the pyruvate and placebo groups. Employing the standard meta-analysis software (RevMan 5.0, 2008), we calculated MDs and 95% CIs. The I^2 statistic was used to test for heterogeneity amongst studies. A funnel plot was used to test for publication bias.

RESULTS

Our searches produced 5007 "hits" of which 9 articles were potentially relevant (see Figure 1). Two trials were excluded

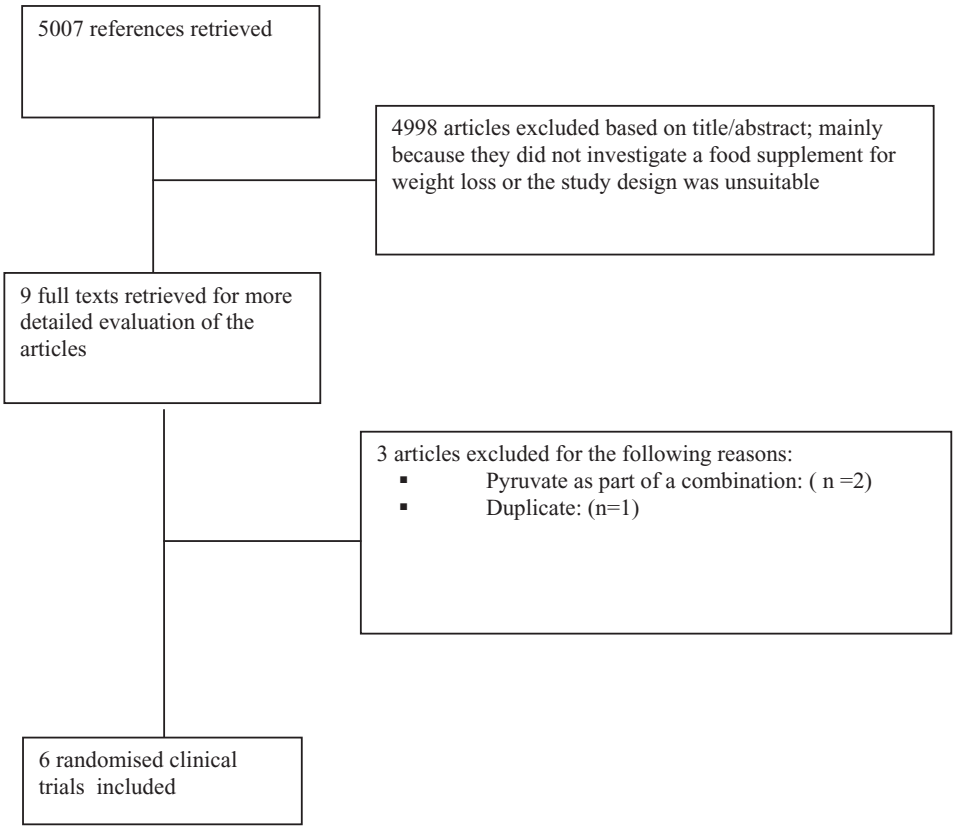

Figure 1 Flow chart showing the process for the inclusion of randomized clinical trials.

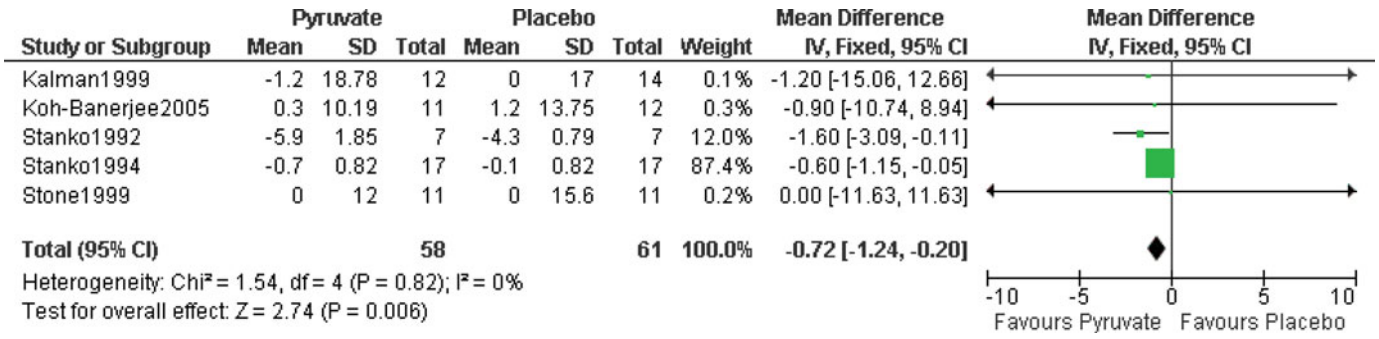

Figure 2 Effect of pyruvate supplementation on body weight. Values are expressed in kilograms (kg). (Color figure available online.)

because pyruvate was combined with dihydroxyacetone as a weight-loss supplement, with pyruvate being only a small fraction of the combinations (Stanko et al., 1992a; Stanko and Arch, 1996). One article (Kalman et al., 1998a) was excluded because the report was a duplicate (abstract) of an RCT (Kalman et al., 1998b) which we included in the review. Thus, 6 RCTs met our inclusion criteria (Koh-Banerjee et al., 2005; Stanko et al., 1992b; Stanko et al., 1994; Kalman et al., 1998b; Kalman et al., 1999; Stone et al., 1999), and were, therefore, included in this systematic review. In total, they included 203 participants. All included RCTs involved overweight and/or obese participants, except in 1 RCT (Stone et al., 1999) where the participants were described as healthy athletes. The key details of the studies included in this systematic review are summarized in Tables 1 and 2.

All RCTs included in this review had important methodological weaknesses (Table 1). Only one study reported adequate randomization (Stanko et al., 1994), and none of the studies reported adequate allocation concealment. No RCT reported performing sample size calculation, and only 1 RCT (Stone et al., 1999) reported appropriate blinding of care providers; while 3 RCTs (Kalman et al., 1999; Koh-Banerjee et al., 2005; Stone et al., 1999) reported adequate blinding of study participants. No RCT reported blinding of outcome assessors. The information on drop-out participants was also poor, and no study reported performing intention-to-treat (ITT) analysis.

One of the RCTs included in the review did not report pre- and postintervention changes in body weight amongst participants in the pyruvate and placebo groups (Kalman et al., 1998b). A forest plot (fixed effect model) of the 5 trials which provided suitable data for changes in body weight is shown in Figure 2. The meta-analysis reveals a small statistically significant difference in body weight loss between pyruvate and placebo (MD: −0.72 kg; 95% CI: −1.24 to −0.21). The I^2 statistic (0%) suggests that heterogeneity may not be important in the analysis. The dosage of pyruvate used differed amongst the trials included in the meta-analysis. A funnel plot (not shown) of these studies showed that they are distributed around a mean, but this does not rule out publication bias.

A forest plot showing the effect of pyruvate on body fat is shown in Figure 3. The meta-analytic results suggest a statistically significant difference in body fat loss between pyruvate and placebo (MD: −0.54 kg; 95% CI: −0.94 to −0.15). The magnitude of this effect is, however, small, and the I^2 statistic of 0% suggests that heterogeneity may not be important in the analysis.

Three RCTs (Stanko et al., 1994; Koh-Banerjee et al., 2005; Stone et al., 1999) reported adverse events. Gastrointestinal adverse events were more common in the pyruvate group in 1 RCT (Stanko et al., 1994), while another RCT (Koh-Banerjee et al., 2005) reported adverse effects of pyruvate on the blood lipid profile. Mild headache was reported as an adverse event in the third RCT (Stone et al., 1999). The remaining 3 RCTs (Stanko et al., 1992b; Kalman et al., 1998b; Kalman et al., 1999) failed to report on adverse events. A total of 19 drop-outs were reported, but there was no report on the reasons for drop-outs, or to which

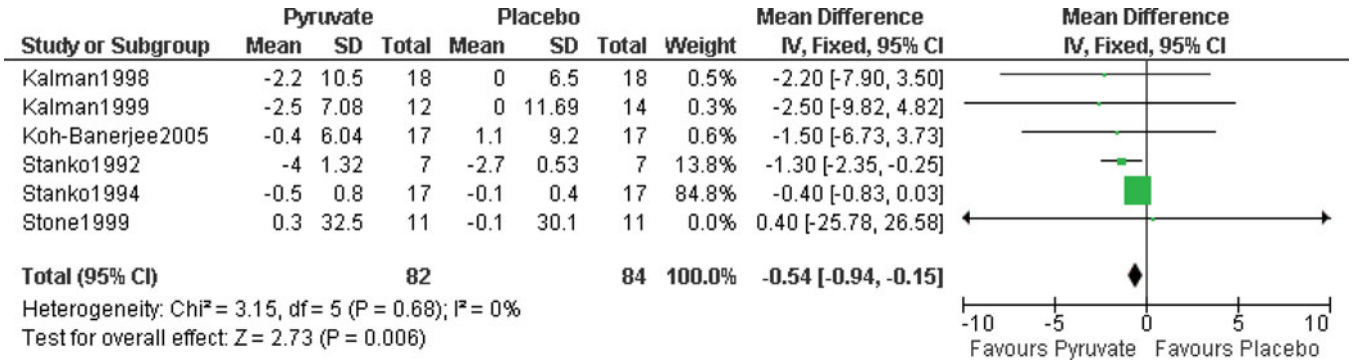

Figure 3 Effect of pyruvate supplementation on body fat. Values are expressed in kilograms (kg). (Color figure available online.)

Table 1 Methodological characteristics of RCTs

First author Year Country	Main outcome(s)	Main diagnoses of participants	Study design	Randomization appropriate?	Allocation concealed?	Sample size determined?	Groups similar at baseline?	Similar follow-up groups?	Outcome assessor blinded?	Care provider blinded?	Patients blinded?	Attrition bias?	ITT analysis?
Stanko 1992b USA	Body composition, energy deficit	Obese subjects	Parallel	Unclear	Unclear	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Unclear	Unclear
Stanko 1994 USA	Body composition, blood lipid profile	Overweight subjects	Parallel	Yes	Unclear	Unclear	Yes	No	Unclear	Unclear	Unclear	Unclear	Unclear
Kalman 1998b USA	Body composition, mood	Healthy, overweight subjects	Parallel	Unclear	Unclear	Unclear	Yes	Yes	Unclear	Unclear	Unclear	Unclear	Unclear
Kalman 1999 USA	Body composition	Healthy, overweight subjects	Parallel	Unclear	Unclear	Unclear	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear
Koh—Banerjee 2005 USA	Body composition, exercise capacity, blood chemistry profile	Healthy, moderately overweight subjects	Parallel	Unclear	Unclear	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	No
Stone 1999 USA	Body composition	Healthy athletes	Parallel	Unclear	Unclear	Unclear	Yes	Yes	Unclear	Yes	Yes	Unclear	Unclear

Table 2 Main results of included RCTs[a]

First author Year	Pyruvate formulation and and daily dose	No. of participants randomized	Age in years	Baseline weight of subjects (kg)	Treatment duration	Main results	Adverse events	Control for lifestyle factors
Stanko 1992b	PYR salts in liquid diet; 30 g	14	Not reported	PYR: 111.0 (25.4) PLA: 104.2 (19.3)	3 weeks	Weight loss was 5.9 (1.85) kg and 4.3 (0.79) kg for PYR and PLA, respectively. Fat loss was 4.0 (1.32) kg and 2.7 (0.53 kg), respectively, for PYR and PLA	Not reported	2100–2400 kcal, then 1015 kcal daily; confined to bed
Stanko 1994	PYR salts as a liquid suppl.; 22–44 g	34	PYR: 56 (12.4) PLA: 58 (12.4)	PYR: 73.6 (11.1) PLA: 75.7 (17.3)	6 weeks	Weight loss was 0.7 (0.82) kg and 0.1 (0.82) kg for PYR and PLA, respectively. Fat loss was 0.5 (0.8) kg & 0.1(0.4) kg, respectively, for PYR and PLA	Gas, bloating, loose stools, diarrhea	1600 kcal daily, nonexhaustive exercise, alcohol intake $\leq$ 80 ml daily
[b]Kalman 1998b	PYR salts as capsules; 6 g	53	PYR: 37.1 (13.6) PLA: 36.4 (8.5)	PYR: 81.0 (17.8) PLA: 72.8 (15.7)	6 weeks	Significant $\downarrow$ in fat mass and % body fat in PYR group ($p < 0.001$); no significant changes in the PLA group for these weight indices	Not reported	2200 kcal daily, exercise
Kalman 1999	PYR capsules; 6 g	26	PYR: 36.5 (10.4) PLA: 39.9 (14.2)	PYR: 76.2 (17.3) PLA: 80.0 (15.7)	6 weeks	Significant $\downarrow$ in body weight, body fat, and % body fat in PYR compared to PLA (all with $p < 0.001$)	Not reported	2000 kcal daily, exercise
Koh—Banerjee 2005	Calcium PYR powder form; 5 g	34	33 $\pm$ 8 for both PYR and PLA groups	PYR: 71.1 (9.4) PLA: 71.9 (12.4)	4 weeks	No significant differences between groups with respect to all weight indices	$\downarrow$HDL cholesterol; $\uparrow$LDL cholesterol; $\uparrow$triacylglycerols	Normal diet, resistance training
[c]Stone 1999	Calcium PYR capsules; 16–23 g	42	PYR: 18.6 (1.99) PLA: 18.3 (1.3)	PYR: 86.9 (12.3) PLA: 88.0 (15.6)	5 weeks	No significant differences between groups with respect to all weight indices	Headache	2421–4747 kcal, weight training, occasional sprinting

[a]where reported, values are presented as means with standard deviations.
[b]study had 3 intervention groups.
[c]study had 4 intervention groups.
Abbreviations: PYR: pyruvate; PLA: placebo; HDL: high-density lipoprotein.

intervention groups the drop-outs belonged to. In 1 RCT (Stone et al., 1999) all 6 drop-outs were reported to have occurred for reasons unrelated to the study.

All RCTs included in this review incorporated lifestyle adjustments into their trial regimen (Table 2). The daily caloric intake of participants ranged from 1015 (Stanko et al., 1992b) to over 4500 kcal (Stone et al., 1999). In 1 study (Stanko et al., 1992b), participants were required to consume a high-caloric diet (2100–2400 kcal daily) for a 3-day run-in period prior to administration of the pyruvate and placebo pills; and then fed a low-caloric diet for 3 weeks. One study did not report the daily caloric intake of subjects (Koh-Banerjee et al., 2005), and 2 studies utilized the services of nutritionists to assess the dietary compliance of study participants (Kalman et al., 1999; Koh-Banerjee et al., 2005). One RCT reported using a food processor to analyze the total daily caloric intake of study participants.

The type of physical activities participants in the different RCTs engaged in also differed. In 1 RCT (Stanko et al., 1992b), the patients were confined to the bed, while participants in another RCT (Stone et al., 1999) underwent weight training, as well as sprinting exercises. In 1 RCT (Koh-Banerjee et al., 2005), the participants performed resistance training, while investigators in the 3 RCTs (Stanko et al., 1994; Kalman et al., 1998b; Kalman et al., 1999) prescribed strict exercise routines. In 1 RCT (Kalman et al., 1998b) exercise physiologists were used to monitor physical activity, while exercise intensity of study participants was calculated in another RCT (Stone et al., 1999).

The dosage of pyruvate used in the included RCTs ranged from 5 g (Koh-Banerjee et al., 2005) to 44 g (Stanko et al., 1994) daily. A dose-response curve revealed a nonlinear, nonsignificant relationship between pyruvate intake and weight loss ($p = 0.41$). Similarly, a plot for body fat (Figure 4) revealed a significant, inverse relationship between pyruvate intake and fat loss ($p = 0.00000$).

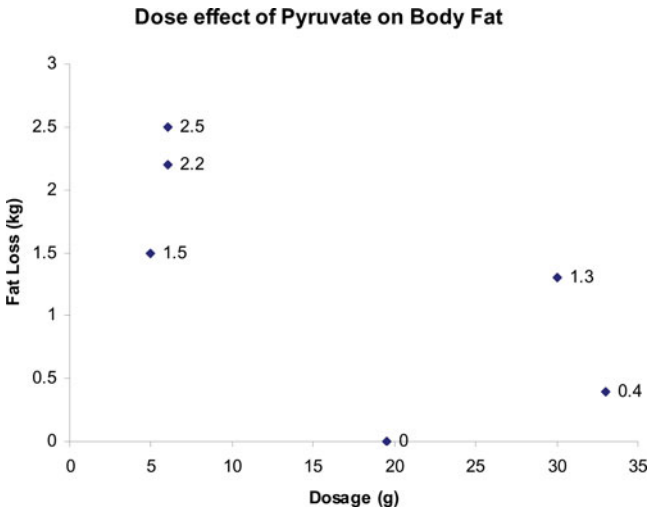

Figure 4 Dose effect of pyruvate on body fat loss. The coefficient of correlation, r was –0.61. (Color figure available online.)

DISCUSSION

The purpose of this systematic review was to assess the efficacy of pyruvate as a weight-loss supplement. The meta-analytic results reveal a statistically significant difference in loss of body weight and body fat favoring pyruvate over placebo. The magnitude of this effect is, however, small, and the clinical relevance is uncertain, as it fails to indicate that the difference in body weight or fat loss is clinically significant. The I^2 values suggest that there is no significant heterogeneity amongst the studies. The results of the meta-analyses should, however, be interpreted with caution, as all the included trials had small sample sizes. Furthermore, all the studies included in this review had 1 or more methodological weaknesses.

Pyruvate is postulated to exert its weight loss effect by increasing the metabolic rates in muscle tissues (Stone et al., 1999). It is also said to have ergogenic potentials, and is, therefore, also used for enhancing endurance capacity (Stanko et al., 1990; Koh-Banerjee et al., 2005). It is claimed that pyruvate may also enhance the fat loss that accompanies physical training (Stone et al., 1999). The findings from our meta-analysis, however, fail to indicate that pyruvate supplementation results in any clinically relevant effects on body composition.

All studies included in this systematic review failed to report whether or not, they carried out a power calculation *ab initio*, and all had small sample sizes. This is of particular concern, as small sample sizes are likely to produce spurious and false positive results. Furthermore, the failure of all the RCTs to report whether or not they performed ITT analyses, coupled with their omission of descriptions of drop-outs/attrition also casts doubts on the validity and reliability of findings. The level of deficient reporting is a poignant reminder for future investigators to adhere to the CONSORT guidelines (Altman et al., 2001; Moher et al., 2001).

The daily dosage of pyruvate varied in the different RCTs. Such variation in doses creates uncertainty about the (minimum) effective dose of pyruvate which might cause weight reduction. The findings from our dose-response graphs seem to suggest that the effects of pyruvate on body weight and body fat are unrelated to dosage. These factors, coupled with the short duration of the RCTs prevent us from being certain about the efficaciousness of pyruvate as a weight-reducing agent.

Lifestyle factors such as diet and physical exercise are important components for successful long-term weight loss (Wadden et al., 2007). Though all the RCTs incorporated some form of lifestyle modifications into their trial regimen, they differed considerably in the amounts of average daily caloric intake, as well as the level of physical activity undertaken by study participants. The extent to which these lifestyle variations influenced the outcome in these studies is at best conjectural.

Though some of the included studies did not report on adverse events, the effect of pyruvate on the blood lipid profile in one of

the included studies (Koh-Banerjee et al., 2005) is a cause for concern. Pyruvate supplementation seemed to dampen the positive effects of exercise on the blood lipid profile of participants in the trial. This contrasts with the report of another RCT (Stanko et al., 1992a) which suggested that pyruvate supplementation has no negative effect on blood lipid profile. This issue warrants further investigation. Gastrointestinal adverse events such as diarrhea and abdominal bloating were also more common in the pyruvate group in 1 RCT (Stanko et al., 1994). Considering the fact that these studies were of short duration, the safety of long-term pyruvate intake seems uncertain. It will be advisable for future investigations to incorporate surveillance time frames into trial designs; to date investigators have tended to stop monitoring for adverse events once the study duration is completed (Ioannidis et al., 2004).

All the RCTs included in the review except 1 (Stone et al., 1999) stated their source of funding. While 2 RCTs (Kalman et al., 1998b; Kalman et al., 1999) were exclusively funded by industry, 3 RCTs (Stanko et al., 1992b; Stanko et al., 1994; Koh-Banerjee et al., 2005) had part-government funding. All RCTs to date, however, have been conducted by a small group of investigators. Larger, independent trials are thus warranted in this regard.

This systematic review does have several limitations. Not all available trials involving the use of pyruvate as a weight-loss supplement may have been identified from our searches. Publication bias may have prevented negative RCTs from getting published. Also the number of studies included in the systematic review is too few, the sample populations were small and variable, and most were poorly conducted. These limitations prevent us from drawing firm conclusions.

CONCLUSION

The evidence from RCTs does not conclusively show that pyruvate intake generates clinically relevant weight loss. Evidence bordering on the safety of pyruvate is also limited. Future trials in this area should make serious attempts at minimizing bias. They should be of adequate sample size and duration. Crucially, they should be reported according to standardized guidelines.

COMPETING INTERESTS

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