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Meta-Analysis Study of the Effects of Yeast Probiotic Supplementation on Milk Production and Energy Corrected Milk of Lactating Dairy Cows

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Abstract

The aim of this study was to use a meta-analytic approach to evaluate the effect of commercially available yeast probiotic "Actisaf® Sc 47" (Saccharomyces cerevisiae CNCM I-4407) produced and marketed by Phileo by Lesaffre on milk performance in dairy cows. Data from 22 trials including 17 with parallel designs and 5 with cross-over designs were collected, and only data with parallel designs were analyzed. From those trials, 4 are published and 13 are from technical reports. In total, 34 comparisons and 1074 dairy cows met the criteria for inclusion in the final analysis of milk yield (MY). For energy corrected milk (ECM), six trials with 12 comparisons and 476 dairy cows met the criteria for inclusion in the final analysis. Because the data are from different trials with different conditions, the statistical model defined includes the fixed effect of the treatment (with vs. without Actisaf® Sc 47) and the random effect of the trial. The meta-analysis showed a moderate heterogeneity for MY and ECM. The random effect meta-analysis showed an estimated mean difference +1.72 kg/d [95% confidence interval (CI): 1.01 to 2.44] and +2.45 kg/d (95% CI: 1.73 to 3.17) for MY and ECM respectively, in favour of Actisaf® Sc 47. The analysis of data without trials conducted under heat stress conditions showed positive effect of Actisaf® Sc 47. The random effect meta-analysis showed an estimated mean difference of +1.69 kg/d [95% CI: 1.24 to 2.14] and +2.92 kg/d (95% CI: 2.45 to 3.40) for MY and ECM respectively, in favour of Actisaf® Sc 47. These observations provide strong evidence that this commercially available yeast probiotic can significantly improve milk performances of dairy cows under different conditions.

Keywords

Milk, Yeast Probiotic, Meta-Analysis

1. Introduction

Since the ban on the use of certain antibiotics as growth promoters in animal feed due to the apparition of antibiotic resistance, the need to find alternatives has accelerated. In response, various additives have been developed and marketed. Among these additives, probiotics have been considerably used over the last 15 years [1]. The use of yeast products such as yeast probiotic in animal nutrition has become widespread and several in vitro and *in vivo* research studies were conducted to understand the mechanism of action and to test production responses. In dairy cow, it was demonstrated that due to oxygen scavenging potential, *Saccharomyces cerevisiae* modulates redox potential and rumen microbiota, consequently allowing them to maintain optimal fermentation conditions [2] [3]. In terms of zootechnical performances, several *in vivo* studies have been conducted to test the effect of different strains and yeast products on milk yield. Despite a large number of scientific studies, the results appear to be inconclusive. Indeed, some studies have shown only a trend [4] [5] or no effect [6] [7] [8] and others have identified significant positive effects [9] [10] [11]. The variation in the results is not well understood and can be explained by different factors such as the experimental conditions [12], the sample size, the climatic conditions, the daily dose of yeast distributed and the yeast strain.

To overcome these sources of variation, meta-analysis has been conducted with different results [13] [14] [15] [16]. In previous meta-analysis studies, yeast probiotic marketed by Phileo by Lesaffre including different strains and doses was considered together with other yeast probiotic to evaluate the global effect of this category of product [15] [16]. However, no meta-analysis containing only the data on yeast probiotic Actisaf® Sc47 at recommended dose of 5 g/d/cow for the specific strain CNCM I-4407 (Lesaffre proprietary strain Saccharomyces cerevisiae CNCM I-4407, Phileo by Lesaffre, Marcq-en-Baroeul, France) was already conducted.

The purpose of the current study was therefore to provide an overview of the effects of Actisaf® Sc 47 on milk yield and energy corrected milk using meta-analytic method.

2. Materials and Methods

2.1. Data Collection

Different steps were used to collect the maximum number of published and unpublished data that studied the effect on dairy cows' performance of commercially available yeast probiotic Actisaf® Sc 47 produced and marketed by Phileo by Lesaffre (Lesaffre proprietary strain Saccharomyces cerevisiae CNCM I-4407, 10^{10} CFU/g). At first, all data from technical reports, registration files and trials conducted on reference farms were identified and collected from the manufacturer. Secondly an exhaustive search in English and French language was carried out using key words such as "live yeast", "probiotics", "dairy cow", "milk yield", "levures vivantes", "levures probiotiques", "vache laitière" in different search engines and scientific journals (ScienceDirect, PubMed, Google Scholar, Journal of Daisy Science, Journal of Animal Science, Livestock Science, Animal) to identify other research papers and reports that may not have been provided by the manufacturer. Also, reference lists of studies investigating the effects of yeast on dairy cow were reviewed for potentially missed studies.

2.2. Selection and Inclusion Criteria

Data were selected if they contained at least one of the following parameters: milk yield (MY) with known standard deviation, energy corrected milk (ECM) with known standard deviation, % or quantity of fat and protein; with a comparison between treatment at the dose of 5×10^{10} CFU/d/cow (corresponding to 5 g/d/cow) and control groups and obtained in lactating dairy cows. In total, 22 studies representing 44 dietary treatments were pooled. Among which 17 used parallel designs and 5 crossover designs (**Figure 1**). Only data with parallel designs were analyzed; studies with crossover designs being more focused on evaluation of parameters linked to rumen fermentation rather than milking performance.

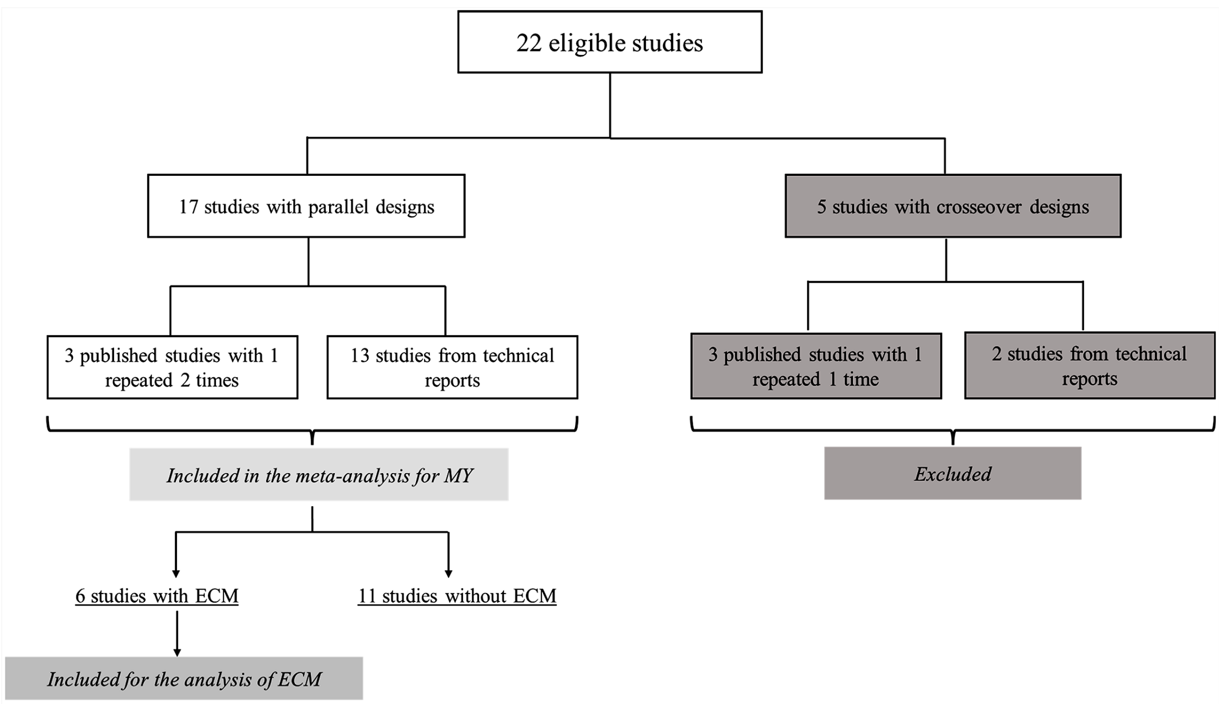

Figure 1. Description of studies collected and included in the meta-analysis.

Each trial contains only two groups (one control without yeast probiotic and one experimental with yeast probiotic). In each trial, the same conditions were used (same breed, stage of lactation, climatic conditions, and barn). Each trial was individually encoded. Some estimates were applied when data were lacking in the publications and when good predictors were available. Energy corrected milk was estimated from the measured milk yield, fat and protein content according to the following equation:

ECM = (0.327 × kg of milk) + (12.95 × kg of fat) + (7.2 × kg of protein) [17].

Standard deviations were calculated from the standard error of the mean by the square root of the sample size if necessary.

2.3. Statistical Analysis

Trials were individually encoded to be used in the model. Two complementary analyses were performed. At first, meta-analysis was performed following the recommendation of [18] using Minitab software. The statistical model applied to the data was:

$$Y_{ijkl} = \mu + Treatment_i + Trial_j + DIM_k + E_{ijkl}$$

where Y_{ijkl} = animal response as explained variable, μ = overall mean, $Treatment_i$ = fixed effect of the treatment (yeast vs. control), $Trial_j$ = random effect of the trial j, DIM_k = day in milk as covariate and E_{ijkl} = random residual error.

For each variable, a graphic verification of data quality was done via boxplot to identify outliers. Outliers were considered for data appearing with an asterisk in the boxplot (and thus for values with ±1.5 interquartile range) and outside the 95% confidence interval of the normality probability plot. This method was accompanied by a verification of normalized residuals (*i.e.*, differences between model-predicted and measured value of the studied parameter, divided by the standard deviation of the residuals' values). For each dependent variable, experiments presenting normalized residuals greater than 2.0 or less than −2 were discarded from the analysis but not from the analyses of other variables.

Secondly, using the same model, size effect of studies included was calculated by mean difference (MD) with 95% confidence interval (CI) using R software (version 4.0.3) with the package meta "General package for meta-analysis" [19]. Heterogeneity among studies was estimated by I^2 value. Heterogeneity can be classified from low to high based on I^2 [20]: low if I^2 value is less than 25%, moderate if I^2 value is between 25% and 50% and high if I^2 value is above 50% = 0.75%. Those results were displayed with a forest plot, and a funnel plot was also done using the same package. The effect was considered significant at $p < 0.05$, considered a tendency toward significance at $p < 0.1$, and non-significant at $p > 0.1$.

3. Results

3.1. Milk Yield: Global Description of the Database and Effect of Yeast Probiotic

For milk yield, a total of twenty-two studies met the inclusion criteria for the meta-analysis. Out of the twenty-two studies, five using latin square design were removed. Studies originated from ten different countries around the world and were conducted between 2009 and 2021 (**Figure 2**). The figure shows the effect of Actisaf®Sc 47 on milk yield in all the trials. The distance between two points within the same trial indicates the importance of the effect of Actisaf® Sc 47. The more the points are distant, the more the effect of the yeast probiotic is important. Overall, 29% of trials (10/17) showed a clear positive effect of Actisaf® Sc 47 on MY varying from 1.3 to 5.4 kg/d which represents a mean increase of 7.5%. There was 24% of trials (4/17) that showed slight positive effect of Actisaf® Sc 47 on MY varying from 0.1 to 0.6 kg/d which represents a mean increase of 1.0%. Only 18% of trials (3/17) showed slight decrease on MY varying from −0.4 to −0.6 kg/d which represents a mean decrease of 1.1%.

Funnel plot did not suggest any bias of publication (**Figure 3**).

The analysis of milk yield showed a moderate level of heterogeneity (I^2 = 42%). The pooled mean difference (MD) obtained with the random effect model was high and significant (1.72; 95% CI: 1.01 - 2.44; $p < 0.001$, **Figure 4**). After the removal of trials conducted under challenged conditions (Moallem *et al.*, 2009 and Mathlouthi *et al.*, 2009) such as heat stress, the effect of Actisaf® Sc 47 remained positive. The pooled MD obtained with the random effect model

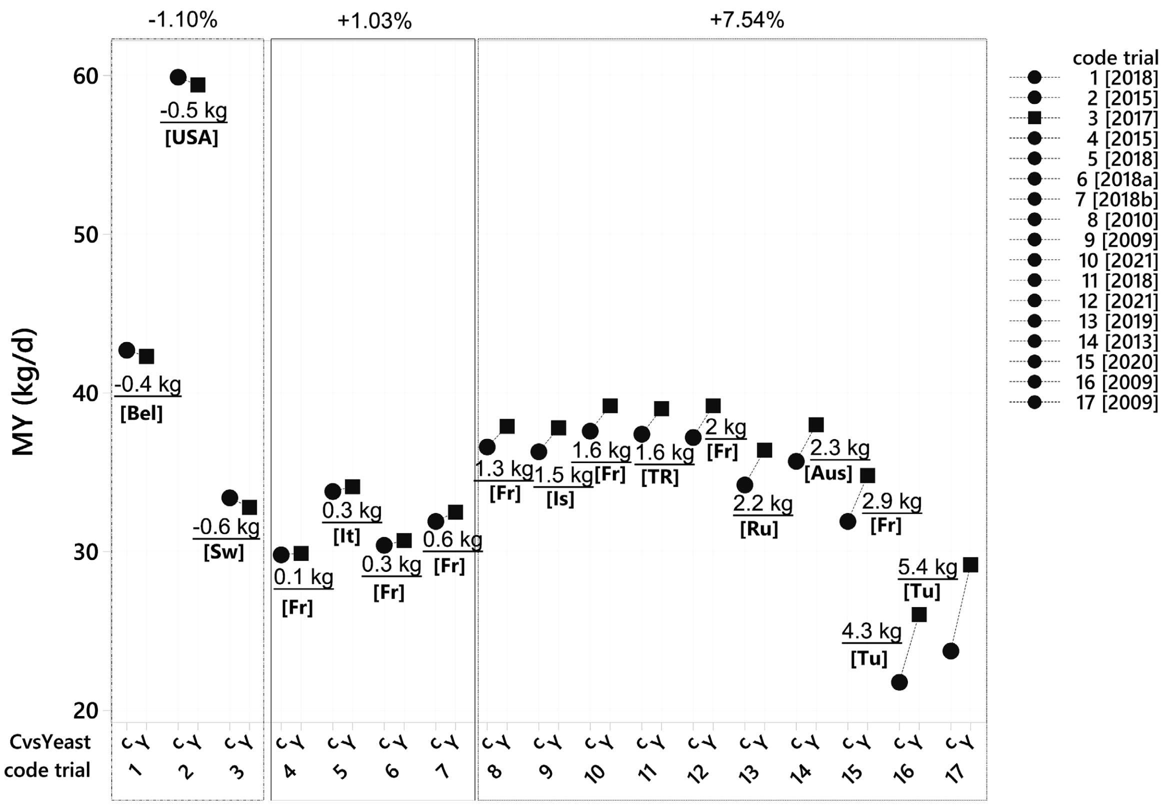

Figure 2. Effect of yeast probiotic at 5 g/cow/d on MY. Each pair of dots represents a trial carried out, and black dots represents control group while the black square the yeast probiotic supplemented group. The country in which the trial was carried out is indicated as followed: USA = United States of America, Jap = Japan, Bel = Belgium, Sw = Switzerland, Fr = France, It = Italy, Isr = Israel, Ru = Russia; TR = Czech Republic, Aus = Australia, Tu = Tunisia.

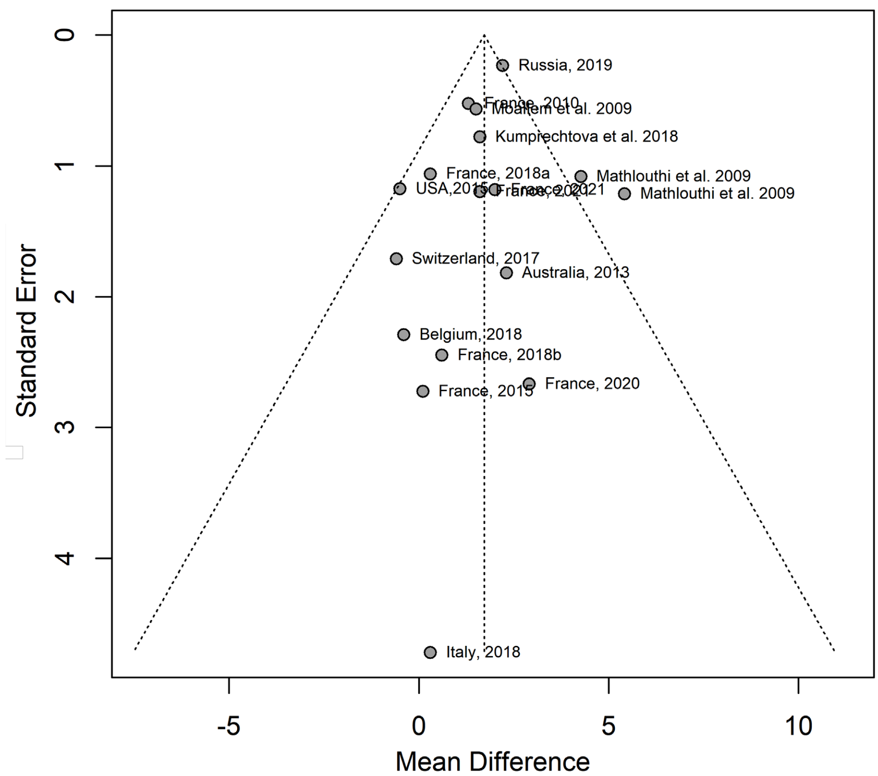

Figure 3. Funnel plot related to milk yield. Funnel plot signifying the symmetrical distribution of observed outcome relative to mean difference of all studies against standard error.

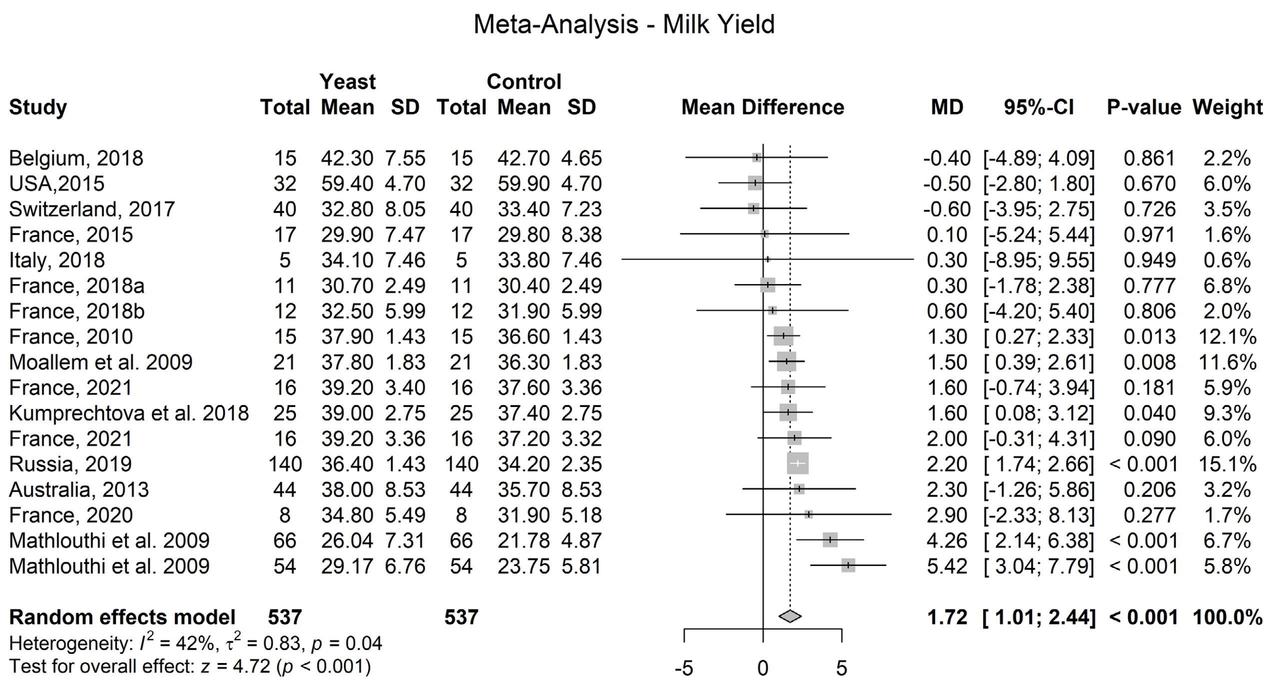

Figure 4. Forest plot of random effects mean difference (MD) and their 95% CI and weights for individual trial for milk yield. Grey squares represent the weighting (by inverse variance) for the represented study, and the horizontal bars represent the 95% CI for the study. The diamond figure center represents the standardized mean, and the width the 95% CI of the overall.

without those trials was high and significant (+1.69 kg; 95% CI: 1.24 - 2.14; $p < 0.001$).

3.2. Energy Corrected Milk: Global Description of the Database and Effect of Yeast Probiotic

For energy corrected milk, six studies met the inclusion criteria for the meta-analysis. Studies were excluded if they used crossover and latin square designs. Studies originated from five different countries around the world and were conducted between 2009 and 2020 (**Figure 5**). All trials (100%, 6/6) showed an increase in ECM varying from 0.2 to 3.1 kg/d which represents a mean increase of 5%.

The funnel plot appears to be balanced suggesting the absence of any bias of study (**Figure 6**).

The analysis of ECM showed a low level of heterogeneity ($I^2 = 32\%$). The pooled mean difference (MD) obtained with the random effect model was high and significant (2.45 kg/d; 95% CI: 1.73 - 3.17; $p < 0.001$, **Figure 7**). After the removal of trials conducted under challenged conditions (Moallem *et al.*, 2009) such as heat stress, the effect of Actisaf® Sc 47 remained positive. The pooled MD abtained with the random effect model without this trial was high and significant (+2.92 kg; 95% CI: 2.45 - 3.40; $p < 0.001$).

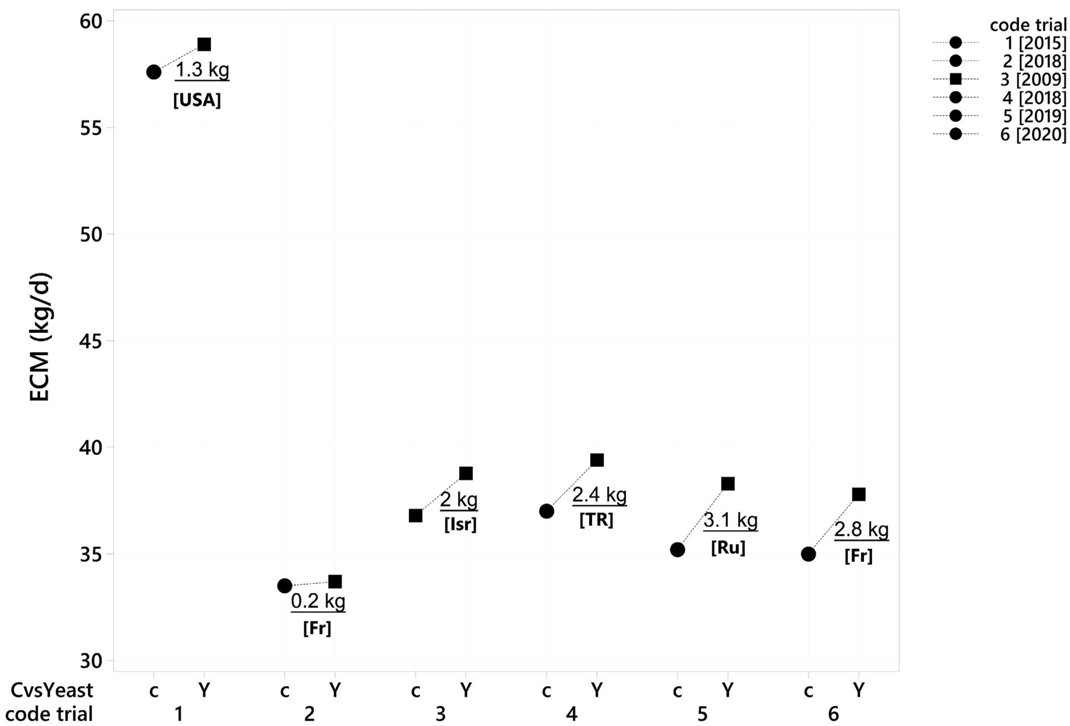

Figure 5. Effect of yeast probiotic at 5 g/cow/d on ECM. Each pair of dots represents a trial carried out, and black dots represents control group while the black square the yeast probiotic supplemented group. The country in which the trial was carried out is indicated as followed: USA = United States of America, Fr = France, Isr = Israel, Ru = Russia; TR = Czech Republic.

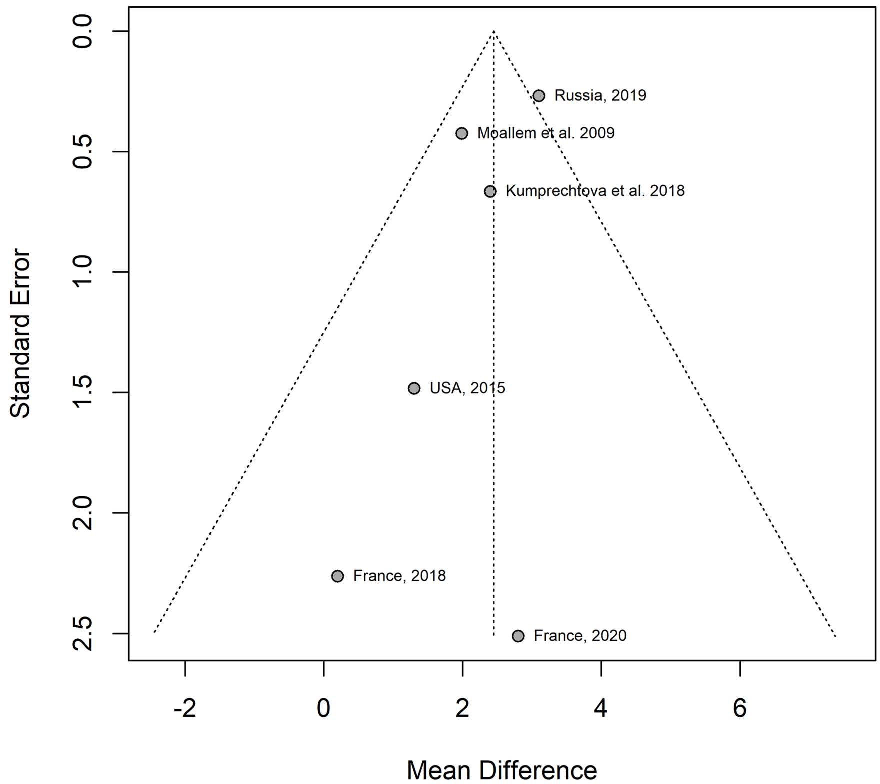

Figure 6. Funnel plot related to energy corrected milk. Funnel plot signifying the symmetrical distribution of observed outcome relative to mean difference of all studies against standard error.

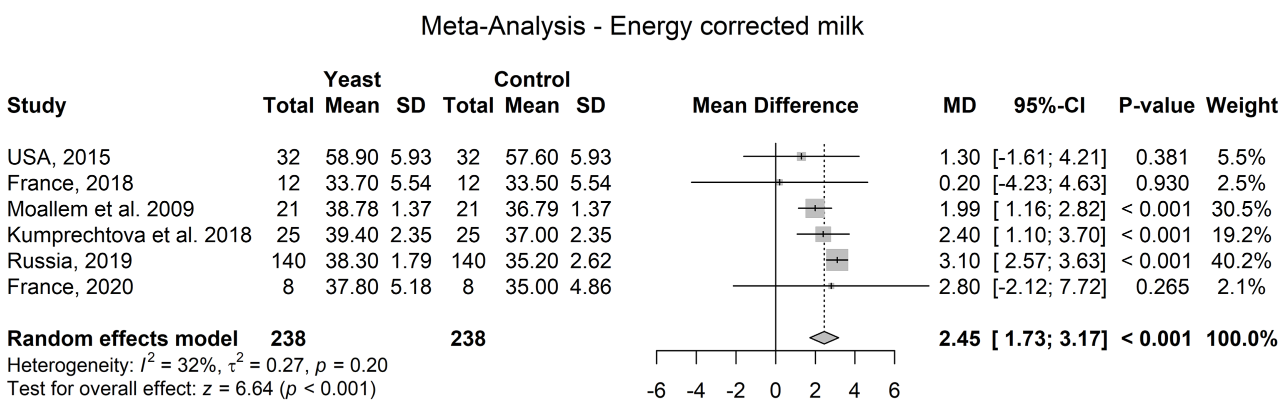

Figure 7. Forest plot of random effects mean difference (MD) and their 95% CI and weights for individual trial for energy corrected milk. Grey squares in the forest plot represent the weighting (by inverse variance) for the represented study, and the horizontal bars the 95% CI for the study. The diamond figure centre represents the standardized mean, and the width the 95% CI of the overall treatment effect. Outcomes displayed on the right of zero represent an increase in energy corrected milk. SD = standard deviation, MD = mean difference, Total = number of animals.

4. Discussion

This meta-analysis investigated the effect of yeast probiotic Actisaf® Sc 47 (*Saccharomyces cerevisiae* CNCM I-4407) produced by Phileo by Lesaffre on MY and ECM in dairy cow. We analyzed heterogeneity which is an important step in meta-analysis as it gives direct information about the quality and the variance within the studies [21]. The I^2 statistics is an indication of the difference between individual study outcomes. The higher the value of I^2, the greater the difference between the results of individual studies. The observed heterogeneity in this study was moderate for the MY and low for ECM. Some factors may affect the response to the yeast product supplementation such as climatic conditions, heat stress, feed quantity and quality [13].

One of the most important bias in meta-analysis studies is publication bias defined as studies in which the observed efficacy of the treatment is much more likely to be reported and published than those in which the observed efficacy is average or poor [22]. Another reason for publication bias could be the tendency for reports produced for or by industry to be only favorable, thereby increasing the magnitude of publication bias [23] [24]. In the present meta-analysis, the effects of the yeast probiotic were studied with peer reviewed paper and industry reports whether positive effects were demonstrated or not to reduce this potential bias.

The effect of yeast probiotic or yeast products has been well studied before via simple individual trials or meta-analysis approach. In this study, yeast probiotic Actisaf® Sc47 supplementation (*Saccharomyces cerevisiae* CNCM I-4407) at 5 × 10^{10} CFU/d corresponding to 5 g/d/head improved MY by 1.72 kg/d. This confirms the observation of [16], who concluded that the addition of yeast (without differentiation between yeast probiotic and yeast culture) increased MY by 0.75 kg/k for a 625 kg live weight cow. More recently, in a review of 18 trials, representing 855 cows in control group and 851 cows in yeast probiotic group, the average increase of MY in supplemented cows was 0.76 kg/d. The same tendency was observed when comparing data from 29 trials using 1606 cows in control group and 1634 cows in yeast culture group with an increase by 0.69 kg/d [15]. By analyzing data from 14 trials, of which 10 correspond to technical reports and 4 to publications, [14] observed an increase in MY by 1.15 kg/d but did not identify an increase in DMI with yeast probiotic supplementation. Moreover, in a review of 14 experiments analyzing the effect of yeast probiotic on milk production, it has been demonstrated that yeast supplementation increased MY by 1.45 L/d and DMI by 0.53 kg/d [25]. Regarding the data of this study, we were not able to analyze other outcomes than MY and ECM. We hypothesized that the increase in MY could be a consequence of better ration valorization and digestion resulting from an improvement in rumen environment [4] [26].

The effect of yeast probiotic on rumen function and metabolism was well studied either in vitro or *in vivo*. It has been shown that yeast probiotic supplementation stimulates digestion [4] [27], stabilizes pH, and promotes microbial population growth Therefore, improvement of MY observed with Actisaf® Sc 47 could be a consequence of improved rumen function [28].

Overall, the present study indicates significant increase of ECM by 2.45 kg/d when supplementing Actisaf® Sc 47. This confirms the results of [29], who observed significant beneficial effects of yeast probiotic on ECM (+1.4 kg/d). Reference [30] conducted a meta-analysis on the effect of yeast probiotic on digestibility and milk performance and observed an increase in ECM by 1.2 kg/d. Our results are consistent with those of [10], who observed positive effect (+1.4 kg/d) of yeast probiotic on ECM during summer. Reference [4] also detected a +0.9 and +5 kg/d increase in ECM when dairy cows were fed 2 dosages of yeast probiotic under heat stress conditions. Energy corrected milk is estimated from the amount of milk, fat and protein and increases each time one of these parameters increases [17].

We hypothesized that the increase in ECM observed with Actisaf® Sc 47 could be a consequence of better MY, protein and especially fat yield. Indeed, several previous studies have shown a positive effect of yeast probiotic on fat yield [10] [15] [31] and protein yield [4] [10] [14]. The observed benefit of supplementing yeast probiotic could be a consequence of higher total volatile fatty acid concentration [9] [32], and their relationship with growth of rumen papillae [33] [34], an increased mitotic index and an inhibition of apoptosis of rumen papillae [15]. All those mechanisms could result in improvement of rumen absorption capacity [35].

The increase of ECM with yeast probiotic observed in our study can be explained by his effect of protein metabolism. [36] indicated that yeast probiotic may reduce dietary nitrogen ruminal degradation and consequently increase rumen undegradable protein (RUP) which is positively correlated to ECM as observed by [37]. Indeed, these authors tested different combinations between rumen degradable (RDP) and undegradable proteins and observed an increase in ECM by 16% when RUP increases from 6% to 8% with the same level of RDP and an increase in ECM by 10% when RDP decreases from 10% to 8% with the same level of RUP (6%).

5. Conclusion

The present meta-analysis demonstrated that supplementation of dairy cows with yeast probiotic Actisaf® Sc 47 (Lesaffre proprietary strain Saccharomyces cerevisiae CNCM I-4407) resulted in significant increases in MY and ECM. The improvement of these two parameters is likely related to improved rumen environment and metabolism. A limit of this work is the lack of data on feed intake and ruminal parameters. Further investigations through studies which would include measurements on rumen metabolism, feed intake and milk performance in the same experiments would likely enhance the analysis of the beneficial effect of this yeast probiotic strain on milk parameters.

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Authors' Contribution

This work was carried out in collaboration among all authors. Author NS and HL collected the data and designed the study. Author NS wrote the first draft of the manuscript. Authors NS, HL and FM performed the statistical analysis. Authors PPP and CB managed the analysis of the study. Authors MB and VN managed the literature searches and supported data collection. All authors read and approved the final manuscript.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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