

# Summary of PubMed studies and related sources on LaKe (lactate-ketone ester)

## Background and what LaKe is

LaKe ("lactate-ketone" ester) is a synthetic dietary supplement that links two metabolic metabolites: the lactate anion produced during intense exercise and (R)-1,3-butanediol, which is converted to beta-hydroxybutyrate (BHB, a ketone body). By chemically linking these compounds, the ester is designed to deliver lactate and ketone bodies simultaneously without the acid or salt loads that prevent high oral doses of lactate and ketone salts. The concept was developed by researchers at Aarhus University, who patented the molecule and co-founded Mmimetika Biosciences to commercialize it <sup>1</sup>.

Regular exercise and fasting increase both lactate and ketone levels. Research shows that lactate serves as a signalling molecule ("exercine") that promotes brain homeostasis and neurogenesis, while ketones are an efficient energy source for the heart and brain. Mmimetika markets their "next generation lactate|ketone" ester as a dietary supplement for metabolic health and longevity, claiming that high levels of lactate and ketones mimic the body's response to hard exercise and fasting <sup>2</sup>. The marketing materials state that the supplements are clear liquids that rapidly release lactate and BHB and can help maintain metabolic control <sup>3</sup>.

## Peer-reviewed preclinical study (Ottosen et al. 2024)

### Design and synthesis

A single peer-reviewed paper currently characterizes LaKe. In the study by Ottosen and colleagues (Journal of Agricultural and Food Chemistry 2024), the researchers designed a neutral primary carboxylic ester of (S)-lactate and (R)-1,3-butanediol that can be hydrolysed to release lactate and BHB. They developed both chemical and chemo-enzymatic methods to produce the ester on multigram scale and showed that it was stable when stored at -15, 0 and 20 °C for two years <sup>4</sup>. In simulated gastric conditions the ester hydrolysed slowly, but hydrolysis proceeded rapidly in simulated intestinal fluid, plasma and in the presence of rat or human hepatocytes <sup>5</sup>. The authors noted that the compound is neither acidic nor salty and can therefore be ingested as a liquid <sup>6</sup>.

### Pharmacokinetics in rats

Eight rats were gavaged with LaKe or placebo, and blood samples were collected for two hours. LaKe raised plasma lactate and BHB concentrations within 15 minutes and they returned to baseline after ~2 hours <sup>7</sup>. A separate extended pharmacokinetic study showed that higher doses (1.125 to 4.5 g kg<sup>-1</sup>) produced dose-dependent increases in BHB and lactate; at the highest dose the BHB concentration remained elevated for eight hours <sup>8</sup>. The ester decreased plasma free fatty acids and increased the appetite-suppressing metabolite N-L-lactoyl-phenylalanine (Lac-Phe) <sup>9</sup>. Rats receiving high doses showed transient reduction in spontaneous activity, whereas moderate doses were well tolerated <sup>10</sup>.

## **Inferences and significance**

The authors concluded that LaKe provides a controlled way to raise both lactate and ketone bodies, thereby mimicking metabolic signals of strenuous exercise and fasting. They suggested that the dual delivery could suppress appetite and free-fatty-acid release and might therefore help manage obesity and type 2 diabetes. The paper discloses that several authors are co-founders of Mmimetika Biosciences and hold a patent on lactate-ketone esters <sup>1</sup>.

## **Ongoing human research**

### **MetaLaKe trial (NCT05917873)**

The only registered clinical trial of LaKe is the double-blind, placebo-controlled, cross-over MetaLaKe study at Aarhus University. Ten adults with obesity will receive 25 mL of LaKe ester or placebo twice daily for 28 days before experimental days <sup>11</sup>. The primary hypotheses are that chronic LaKe supplementation will improve insulin sensitivity and cardiac output compared with placebo <sup>12</sup>. Secondary endpoints include appetite sensations, gastric emptying, lipolysis, hormonal responses (GLP-1, Lac-Phe), body composition and safety <sup>13</sup>. The study aims to determine whether chronic LaKe intake modulates metabolic and cardiovascular parameters without requiring exercise. No human data have been published yet.

### **Network-of-Care summary**

A network-of-care summary of the MetaLaKe trial notes that oral lactate and BHB separately suppress appetite and inhibit lipolysis in obese adults. The trial therefore asks whether the combined LaKe ester affects insulin sensitivity, appetite, gastric emptying, lipolysis and cardiac function <sup>13</sup>. Participants will ingest LaKe or placebo twice daily for 28 days before experimental days <sup>13</sup>. Sponsors include the University of Aarhus and Novo Nordisk.

## **Marketing claims and lay media coverage**

### **Longevity.Technology article (Oct 2024)**

A Longevity.Technology article describes LaKe as “a combination of lactate and ketone ester promising to enhance energy metabolism” <sup>14</sup>. The article states that the compound mimics some exercise-induced effects: improved cellular metabolism, better fat and sugar processing, enhanced mitochondrial function and improved energy balance <sup>15</sup>. It claims that LaKe lowers oxidative stress and inflammation and could benefit those unable to exercise <sup>16</sup>. The article cautions that human effects are unknown and that more research is needed before LaKe can be used broadly <sup>17</sup>.

### **Phys.org / Aarhus University news (Oct 2024)**

A news release explains that LaKe induces a metabolic state equivalent to running 10 km on an empty stomach <sup>18</sup>. It notes that raising lactate and ketone levels increases an appetite-suppressing hormone and lowers free fatty acids, which could reduce the risk of metabolic syndrome <sup>19</sup>. Researchers emphasize that the effect cannot be achieved through diet alone due to unwanted salt and acid loads and that LaKe offers a way to control lactate and ketone levels safely <sup>20</sup>. The article suggests the supplement could benefit

people unable to exercise or those with weak hearts and hints at potential applications in brain trauma, Parkinson's and dementia <sup>21</sup> . Human trials are underway <sup>22</sup> .

## Portuguese article “LaKe: a nova pílula do exercício?”

A commentary in the Brazilian newspaper *O Imparcial* describes LaKe as an acronym for the union of lactate and ketone bodies. The author explains that lactate is produced by muscles during exercise and acts as an “exercine” that regulates metabolism, while the liver produces ketone bodies such as BHB during prolonged effort <sup>23</sup> . Exercise also stimulates the production of  $\beta$ -aminoisobutyric acid (BAIBA). Studies cited in the article report that lactate promotes angiogenesis and neurogenesis and helps maintain brain homeostasis and prevent depression, whereas ketone bodies support neuroprotection and cognitive functions <sup>23</sup> . When rats ingested LaKe, blood lactate and BHB increased and this was associated with higher brain-derived neurotrophic factor (BDNF), GLP-1 and Lac-Phe levels, which decrease hunger <sup>23</sup> .

## MDLinx analysis

An MDLinx article titled “A pill to replace exercise?” summarizes the preclinical findings and highlights cautionary perspectives from endocrinologist Dr Srividya Kidambi. The article notes that LaKe raised lactate and ketone levels in rats, leading the authors to claim it could mimic exercise and fasting <sup>24</sup> . Dr Kidambi acknowledges potential benefits for sedentary individuals and patients with dementia or Parkinson's disease <sup>25</sup> but stresses that the research is preliminary and that LaKe only mimics the metabolic pathways of exercise, not the mental or social benefits <sup>26</sup> . She warns that long-term elevation of lactate and ketone levels may have unknown consequences and cautions against labelling LaKe as an “exercise pill” <sup>27</sup> .

## Mmimetika marketing

The Mmimetika website presents LaKe supplements as “next generation lactate | ketone esters” that imitate the body's natural response to hard exercise and fasting <sup>2</sup> . They claim the products are clear liquids that rapidly release lactate and BHB and represent the only safe solution for achieving high levels of both metabolites without unwanted salt intake <sup>28</sup> . The site states that these non-medicinal supplements provide general support for metabolic control and longevity <sup>29</sup> . It distinguishes LaKe from other ketone products and promises commercial launch in 2026–27 <sup>30</sup> .

## Other studies involving lactate and ketones

While no other PubMed studies currently investigate LaKe specifically, several publications offer context for potential effects and risks of elevated lactate and ketone levels:

- **Cardiac perfusion study (Seefeldt et al., 2024).** A study on ex vivo heart transplantation perfusion tested the effect of BHB supplementation. LaKe was not investigated, but the authors disclosed that two investigators hold a patent for a combined lactate-ketone ester <sup>31</sup> . This indicates ongoing interest in using combined lactate and ketone delivery to support organ function.
- **Cancer cell “stemness” (Martinez-Outschoorn et al., 2011).** An earlier study using breast cancer models showed that high-energy metabolites such as lactate and ketones fuel tumor growth and metastasis by promoting oxidative mitochondrial metabolism. Culturing breast cancer cells with lactate or BHB increased expression of gene profiles associated with stemness <sup>32</sup> . The lactate- and

ketone-induced gene signatures predicted poor clinical outcomes and promoted tumor growth and metastasis in xenograft models <sup>33</sup>. These findings raise theoretical concerns that chronically elevated lactate and ketone levels could support cancer progression.

## Potential performance applications and “exercise pill” concept

- **Mechanistic rationale:** By simultaneously increasing lactate and ketone concentrations, LaKe aims to mimic the metabolic environment of intense exercise or fasting. In rats, LaKe decreased free fatty acids and increased Lac-Phe <sup>9</sup>, which is known to suppress appetite and may contribute to weight control. Ketones are a preferred fuel for the heart and brain; lactate has been implicated in angiogenesis, neurogenesis and neuroprotection <sup>23</sup>. A dietary supplement that raises both could, theoretically, improve endurance, recovery and cognitive function without physical exertion. Marketing materials propose that LaKe’s dual action can “fully mimic” the body’s response to exercise <sup>30</sup>.
- **Performance claims:** Lay articles claim that LaKe induces a metabolic state equivalent to running 10 km at high speed on an empty stomach <sup>18</sup> and that it improves mitochondrial function, fat oxidation and glucose use <sup>15</sup>. They suggest potential use as an “exercise pill” for athletes or patients with limited capacity for exercise. However, these assertions are based on rodent data; no studies have assessed exercise performance, endurance or recovery in humans.
- **Expert caution:** Dr Kidambi and other commentators stress that LaKe can only mimic certain metabolic pathways of exercise. Exercise confers multiple benefits including muscle strengthening, cardiovascular adaptation, mental health and social interaction, which cannot be replicated by a supplement <sup>26</sup>. They caution that long-term safety and the risk of dependency or tolerance remain unknown <sup>27</sup>. In rats, high doses transiently reduced activity <sup>10</sup>, highlighting potential adverse effects at elevated intake.

## Health risks and longevity considerations

### Potential risks

1. **Unknown long-term effects:** LaKe has only been tested acutely in rats. No chronic toxicity data exist. Elevated lactate and ketone concentrations could strain acid-base homeostasis or lead to electrolyte imbalances. Exogenous ketone supplements sometimes cause gastrointestinal discomfort; whether LaKe produces similar effects is unknown.
2. **Cancer risk:** The 2011 study found that lactate and ketones promote cancer cell “stemness” and metastasis <sup>32</sup>. While this study did not involve LaKe, it suggests that chronic elevation of these metabolites may support tumor progression. Patients with cancer or high cancer risk should therefore exercise caution.
3. **Reduced lipolysis and altered metabolism:** LaKe suppresses lipolysis and free-fatty-acid release in rats <sup>9</sup>. Chronic inhibition of fat mobilization could interfere with normal energy balance. The esters may also modify insulin sensitivity and appetite, the long-term consequences of which remain unclear.

4. **High-dose side effects:** At high doses LaKe caused transient reductions in activity in rats <sup>10</sup>. This could reflect central nervous system effects or metabolic stress. Without human data, safe dosing thresholds cannot be defined.

## Longevity and therapeutic potential

- **Metabolic health:** Raising ketones and lactate may mimic benefits of fasting and exercise. In rats, LaKe increased BHB and lactate without significant side effects at moderate doses <sup>7</sup>. If similar effects occur in humans, LaKe could become a tool for improving insulin sensitivity, reducing appetite and supporting weight management.
- **Cardiovascular benefits:** Ketone bodies are efficient fuel for the failing heart, and raising BHB via exogenous supplements improves cardiac output in some studies. LaKe's ability to elevate both lactate and BHB might improve cardiac energetics; this is one of the hypotheses tested in the MetaLaKe trial <sup>12</sup>.
- **Neurological benefits:** Lactate acts as an alternative brain fuel and stimulates BDNF. Ketones provide neuroprotection and may support cognition. Marketing materials claim LaKe enhances neurogenesis and cognitive function <sup>23</sup>. The upcoming human studies will need to evaluate whether such effects occur.

## Conclusion

A single peer-reviewed study has demonstrated that LaKe, a simple ester linking lactate and (R)-1,3-butanediol, can be synthesized in bulk and rapidly hydrolyses to release lactate and BHB. In rats, acute administration raises lactate and ketone levels, suppresses free-fatty-acid release and increases appetite-suppressing hormones <sup>9</sup>. While these findings are promising and have spurred media headlines about an “exercise pill,” there is currently no human evidence that LaKe improves exercise performance or metabolic health. The ongoing MetaLaKe trial will provide the first data on safety and metabolic effects in humans <sup>12</sup>. Experts caution that LaKe can only mimic a subset of exercise's metabolic benefits and that long-term safety and effects on cancer risk remain unknown <sup>26</sup>. Until rigorous clinical trials demonstrate clear benefits and safety, LaKe should be regarded as an experimental tool rather than a proven exercise replacement.

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<sup>1</sup> <sup>4</sup> <sup>5</sup> <sup>7</sup> <sup>8</sup> <sup>9</sup> <sup>10</sup> Preparation and Preclinical Characterization of a Simple Ester for Dual Exogenous Supply of Lactate and Beta-hydroxybutyrate - PMC

<https://pmc.ncbi.nlm.nih.gov/articles/PMC11403612/>

<sup>2</sup> <sup>3</sup> <sup>6</sup> <sup>28</sup> <sup>29</sup> <sup>30</sup> Mmimetika Biosciences – Next generation lactate | ketones

<https://mmimetika.com/>

<sup>11</sup> <sup>12</sup> SAP\_MetaLaKe\_final

[https://cdn.clinicaltrials.gov/large-docs/73/NCT05917873/SAP\\_000.pdf](https://cdn.clinicaltrials.gov/large-docs/73/NCT05917873/SAP_000.pdf)

<sup>13</sup> San Mateo Clinical Trial Metabolic Effects of Four-week Lactate-ketone Ester Supplementation

<https://aging.networkofcare.org/sanmateo/CommunityResources/ClinicalTrials/Detail/NCT05917873>

<sup>14</sup> <sup>15</sup> <sup>16</sup> <sup>17</sup> LaKe: The lactate-ketone combo that delivers exercise-like benefits without the workout

<https://longevity.technology/clinics/lake-the-lactate-ketone-combo-that-delivers-exercise-like-benefits-without-the-workout/>

18 19 20 21 22 New molecule can mimic the effects of fasting and exercise

<https://phys.org/news/2024-10-molecule-mimic-effects-fasting.html>

23 LaKe: a nova pílula do exercício? | O Imparcial

<https://www.imparcial.com.br/noticias/lake-a-nova-pilula-do-exercicio%2C69947>

24 25 26 27 A pill to replace exercise? It's in the works, but how close to 'perfect' can science get it? |

MDLinx

<https://www.mdlinx.com/article/a-pill-to-replace-exercise-its-in-the-works-but-how-close-to-perfect-can-science-get-it/GTQiXmcQA8xziP5RIVB7U>

31 Effects of ketone body 3-hydroxybutyrate on cardiac and mitochondrial function during donation after circulatory death heart transplantation - PMC

<https://pmc.ncbi.nlm.nih.gov/articles/PMC10774377/>

32 33 Ketones and lactate increase cancer cell “stemness”, driving recurrence, metastasis and poor clinical outcome in breast cancer: Achieving personalized medicine via metabolo-genomics - PMC

<https://pmc.ncbi.nlm.nih.gov/articles/PMC3117136/>