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Risk assessment of D-Ribose (revised)

Opinion of the Panel Food Additives, Flavourings, Processing Aids, Materials in Contact with Food, and Cosmetics of the Norwegian Scientific Committee for Food and Environment

Report from the Norwegian Scientific Committee for Food and Environment (VKM) 2020: 11
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Risk assessment of D-ribose (revised)

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Competence of VKM experts

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Summary

The Norwegian Scientific Committee for Food and Environment (Vitenskapskomiteen for mat og miljø, VKM) has revised the risk assessment of D-ribose (VKM, 2016). NFSA requested a risk assessment of the doses 3100 and 6200 mg/day of D-ribose in food supplements for the age groups children (10 to <14 years), adolescents (14 to <18 years) and adults (≥18 years) (VKM, 2016). The present assessment is a revision, and it is based on additional literature (Thompson et al., 2014) included in the "Statement on the safety of D-ribose" (EFSA, 2018).

A single daily dose of 3100 mg or 6200 mg of D-ribose corresponds to 71.4 or 142.6 mg/kg bw per day for children (10 to <14 years), 50.6 or 101.1 mg/kg bw per day for adolescents (14 to <18 years) and 44.3 or 88.6 mg/kg bw per day for adults (≥18 years).

In the previously published risk assessment (VKM, 2016), based on human studies, a dose of 20 000 mg/day of D-ribose (corresponding to 286 mg/kg bw per day in a 70 kg adult) was identified as the point of departure (POD, described as "value for comparison" in VKM, 2016). Note that this value was not considered to be a health-based guidance value. In this revised assessment, one additional study of D-ribose in humans is included (Thompson et al., 2014). Based on this study the POD was revised, and the risk associated with daily intake of a dose of 3100 mg or 6200 mg D-ribose was re-evaluated. Thompson et al. (2014) reported transient symptomatic hypoglycaemia in a female adult of 53 kg following intake of a single dose of 10 000 mg D-ribose. No effects were observed at a single dose of 5000 mg D-ribose. The revised POD is a total dose of 10 000 mg/day given as single doses of maximum 5000 mg a minimum of 5 hours apart.

No human studies on children (10 to <14 years) and adolescents (14 to <18 years) were identified. In the risk characterisation, a tolerance as for adults, based on body weight, was assumed for children and adolescents.

The margin of exposure (MOE) approach, i.e. the ratio of the POD for a single dose to the exposure, was used for the risk characterisation. The MOEs for a single daily dose of 3100 mg D-ribose are 1.0, 1.4 and 1.6 for children (10 to <14 years), adolescents (14 to <18 years) and adults (≥18 years), respectively. The MOEs for a daily dose of 6200 mg D-ribose given as a single dose are 0.5 for children (10 to <14 years), 0.7 for adolescents (14 to <18 years) and 0.8 for adults (≥18 years).

Conclusions

As the MOEs for a daily dose of 6200 mg D-ribose given as a single dose are below 1.0 for children (10 to <14 years), adolescents (14 to <18 years) and adults (≥18 years) there is a risk of experiencing hypoglycaemia. Therefore, we conclude that a daily single dose of 6200 mg of D-ribose in food supplements may represent a risk of adverse health effects in these age groups.

For a daily single dose of 3100 mg D-ribose in food supplements the MOE is 1.0 for children (10 to <14 years). As the calculated exposure is based on a mean body weight for children and there were no available studies on children, we conclude that a daily single dose of 3100 mg of D-ribose in food supplements may represent a risk of adverse health effects for children (10 to <14 years).

For a daily single dose of 3100 mg D-ribose in food supplements the MOEs are 1.4 for adolescents (14 to <18 years) and 1.6 for adults (≥18 years). We conclude that it is improbable that a daily single dose of 3100 mg D-ribose in food supplements causes adverse health effects in adolescents (14 to <18 years) and adults (≥18 years).

Key words: Adverse health effect, D-ribose, food supplement, hypoglycaemia, negative health effect, Norwegian Food Safety Authority, Norwegian Scientific Committee for Food and Environment, other substances, risk assessment, VKM.

Sammendrag på norsk

Vitenskapskomiteen for mat og miljø (VKM) har revidert en tidligere risikovurdering av D-ribose (VKM, 2016). Risikovurderingen av D-ribose ble gjort på oppdrag fra Mattilsynet, og VKM ble bedt om å vurdere inntak av dosene 3100 mg per dag og 6200 mg per dag av D-ribose i kosttilskudd for aldersgruppene barn (10 til <14 år), ungdom (14 til <18 år) og voksne (>18 år) (VKM, 2016). I denne revisjonen er ny litteratur (Thompson et al., 2014) tatt med fra «Statement on the safety of D-ribose» (EFSA, 2018) .

En daglig enkeltdose av D-ribose på 3100 mg tilsvarer 71,4, 50,6 og 44,3 mg/kg kroppsvekt per dag for henholdsvis barn (10 til <14 år), ungdom (14 til <18 år) og voksne (≥ 18 år). En daglig enkeltdose på 6200 mg tilsvarer 142,6, 101,1 og 88,6 mg/kg kroppsvekt per dag for de samme aldersgruppene.

I risikovurderingen fra 2016 ble en dose på 20 000 mg per dag, basert på humanstudier, brukt som referansepunkt for toksisitet (tilsvarende 286 mg/kg kroppsvekt per dag for en voksen person på 70 kg). I denne reviderte vurderingen som inkluderer en ny studie (Thompson et al., 2014), ble risikoen ved et daglig inntak av D-ribose i enkeltdoser på 3100 mg og 6200 mg vurdert på nytt. Revisjonen er basert på rapportert symptomatisk hypoglykemi hos en voksen kvinne på 53 kg ved en enkeltdose på 10 000 mg D-ribose, mens ingen negative effekter ble observert ved en enkeltdose på 5000 mg (Thompson et al., 2014). Det reviderte referansepunktet for toksisitet er en total dose på 10 000 mg/dag gitt som enkeltdoser på maksimalt 5000 mg med minst 5 timers mellomrom.

Ingen humane studier på barn (10 til <14 år) og ungdom (14 til <18 år) var tilgjengelige. Vi antok at disse aldersgruppene har samme toleranse som voksne basert på kroppsvekt.

I risikokarakteriseringen beregnet vi eksponeringsmarginen, det vil si forholdet mellom referansepunktet for toksisitet og eksponeringen. En enkelt daglig dose på 3100 mg D-ribose gir eksponeringsmarginer som er henholdsvis 1,0, 1,4 og 1,6 for barn (10 til <14 år), ungdom (14 til <18 år) og voksne (≥18 år). For en enkelt daglig dose på 6200 mg D-ribose er disse 0,5 for barn (10 til <14 år), 0,7 for ungdom (14 til <18 år) og 0,8 for voksne (≥18 år).

Konklusjoner

Ettersom eksponeringsmarginene for en daglig enkeltdose på 6200 mg D-ribose i kosttilskudd er lavere enn 1,0 kan det være en risiko for hypoglykemi hos barn (10 til <14 år), ungdom (14 til <18 år) og voksne (≥18 år). Det konkluderes derfor at en daglig enkeltdose på 6200 mg D-ribose i kosttilskudd kan utgjøre en risiko for negative helseeffekter hos barn (10 til <14 år), ungdom (14 til <18 år) og voksne (≥18 år).

Ettersom den beregnede eksponeringen er basert på gjennomsnittlig kroppsvekt for barn samt at det ikke var tilgjengelig studier på barn, konkluderer VKM at en daglig enkeltdose på

3100 mg D-ribose fra kosttilskudd med eksponeringsmargin på 1,0 kan utgjøre en risiko for negative helseeffekter hos barn (10 til <14 år).

For en daglig enkeltdose på 3100 mg D-ribose i kosttilskudd er eksponeringsmarginene for ungdom (14 til <18 år) og voksne (≥18 år) henholdsvis 1,4 og 1,6. Ut i fra dette konkluderte VKM at det er lite sannsynlig at en daglig enkeltdose på 3100 mg D-ribose i kosttilskudd vil forårsake negative helseeffekter hos ungdom (14 til <18 år) og voksne (≥18 år).

Abbreviations and glossary

Abbreviations

ADME	- absorption, distribution, metabolism and excretion
bw	- bodyweight
EFSA	- European Food Safety Authority
NFSA	- Norwegian Food Safety Authority
VKM	- Norwegian Scientific Committee for Food and Environment

Glossary

"Other substances"
A substance other than a vitamin or mineral that has a nutritional or physiological effect (The European Parliament and the Council of the European Union, 2006).

"Negative health effect" and "adverse health effect"
VKM uses the definition endorsed by EFSA for "adverse effect": a change in morphology, physiology, growth, development, reproduction or life span of an organism, system or (sub)population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress, or an increase in susceptibility to other influences (EFSA, 2006; WHO, 1994).

Point of departure (POD)
The point on a dose–response curve established from experimental data used to derive a safe level (EFSA Glossary). The point of departure was described as "value for comparison" in VKM, 2016. Note that this value is not considered to be a health-based guidance value.

Terms of reference as provided by the Norwegian Food Safety Authority

For the risk assessment of D-ribose published in 2016 (VKM, 2016), the terms of reference were as follows:

The Norwegian Food Safety Authority (NFSA) has requested the Norwegian Scientific Committee for Food and Environment (VKM) to assess the safety of D-ribose in food supplements at the following doses: 3100 mg/day and 6200 mg/day. The safety assessments of "other substances" present in food supplements shall be carried out for a general population, ages 10 years and above.

Assessment

1 Introduction

The present assessment is a revision of the previous VKM risk assessment of D-ribose (VKM, 2016), and additional literature from the "Statement on the safety of D-ribose" (EFSA, 2018) is included.

Detailed information with regard to the previous VKM assessment of D-ribose (VKM, 2016) will not be included in the present assessment, which will focus on the revised parts.

The following is text adapted from VKM (2016):

"Other substances" are described in the food supplement directive 2002/46/EC *as substances other than vitamins or minerals that have a nutritional and/or physiological effect*, and may be added to food supplements or e.g. energy drinks (The European Parliament and the Council of the European Union, 2006).

D-ribose is present in all living cells as it is a component of the genetic material RNA and also involved in cellular metabolism. D-ribose is synthesized in all cells, and it has been estimated that the daily endogenous production of D-ribose ranges from 2.7 g/day (women) to 16.5 g/day (men) (Bioenergy Life Science Inc, 2008). The total dietary intake of D-ribose is not known. In this risk assessment, daily intakes of 3100 and 6200 mg/day are assessed.

D-ribose is an ingredient in food supplements sold in Norway. In 2016, VKM published a risk assessment of 3100 and 6200 mg/day of D-ribose in food supplements for the age groups children (10 to <14 years), adolescents (14 to <18 years) and adults (≥18 years). Other sources of D-ribose, such as foods and cosmetics, were not included.

1.1 Limitations

The risk assessment regards the substance D-ribose *per se* and no specific products.

Documentation of any claimed beneficial effects from D-ribose has not been evaluated, but merely possible adverse effects at specified doses used in Norway. Thus, potential high intake consumer groups of the substance may not be identified and included in this assessment.

For risk assessments of macronutrients (i.e. fat, carbohydrate, protein or their substitutes) nutritional as well as toxicological aspects may be considered (Borzelleca, 1996; Dybing et al., 2002; Munro et al., 1996). In the present risk assessment, potential nutritional effects of D-ribose were not specifically evaluated.

2 General information

The following is text adapted from VKM (2016):

D-ribose (CAS no. 50-69-1, EINECS no. 200-059-4) is a naturally occurring carbohydrate, a five carbon monosaccaride. It is an aldopentose due to the aldehyde functional group, and the molecular formula is $C_5H_{10}O_5$. The structural formulas are shown in Figure 2-1.

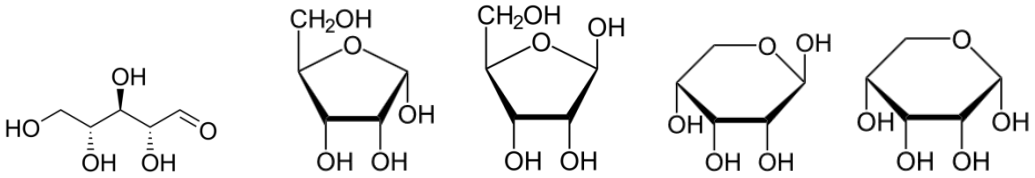

Figure 2-1. The structural formulas of the 5 isomers of D-ribose (from left: open chain, α-D-ribopyranose, β-D-ribopyranose, α-ribofuranose and β-ribofuranose).

D-ribose is a component of the genetic material RNA and is synthesized in all living cells via the pentose phosphate pathway. D-ribose, in the form of ribonucleoside diphosphate, is converted to deoxyribonucleoside diphosphate, precursor molecules for DNA. D-ribose is also a structural component of adenosine triphosphate (ATP), the primary source of cellular energy and a key component of riboflavin (i.e. vitamin B_2) (Griffiths et al., 2007a; Griffiths et al., 2007b). The estimated endogen synthesis of D-ribose is 2.7 g/day (women) and 16.5 g/day (men) (Bioenergy Life Science Inc, 2008). D-ribose is available in small amounts in the diet via ripe fruits and vegetables (Dhanoa and Housner, 2007). It is also an ingredient in food supplements, some so-called energy drinks and in cosmetics as skin conditioner and humectant.

3 Absorption, distribution, metabolism and excretion (ADME)

The following is text adapted from VKM (2016):

Orally administered D-ribose is generally thought to be absorbed in the small intestine by passive diffusion. Absorption rates after oral ingestion of doses up to 200 mg/kg bw per hour (administered for 5 hours) have been shown to range from 87.8 to 99.8% in humans (Gross et al., 1989). Diffusion capacity of D-ribose in the small intestine can be exceeded both in humans and rodents, depending on the amount ingested and other dietary components. Unabsorbed D-ribose passes on to the large intestine where it undergoes fermentation and/or excretion in faeces (Griffiths et al., 2007b). Once absorbed, D-ribose is phosphorylated and enters the pentose phosphate pathway of glucose metabolism as a substrate for purine and pyrimidine biosynthesis. When pentose phosphates are not needed for purine nucleotide synthesis in muscle, or when ribose is present in excess amounts, pentose phosphates are recycled through glycolysis mainly in the liver via conversion into fructose-6-phosphate, fructose-1,6-bisphosphate (to a lesser degree), and glyceraldehyde-3-phosphate, eventually to form CO_2 and water and yielding energy via ATP turnover. The metabolism of D-ribose in humans following intravenous administration indicates that D-ribose is rapidly and extensively metabolised via the pentose phosphate pathway. These data also suggest that D-ribose induces a lowering of blood glucose, presumably by the competitive effect on phosphoglucomutase, thereby preventing metabolism of glycogen to glucose in the liver (Segal and Foley, 1958).

4 Hazard identification and characterisation

4.1 Mutation and genotoxicity studies

No revision of this chapter is performed. The conclusion in VKM (2016) was as follows: "All results from the mutagenicity and genotoxicity tests were negative". For further information, please see VKM (2016).

4.2 Toxicological data/Adverse effects

4.2.1 Human studies

Five human studies on adverse health effects of D-ribose were included in the previous assessment by VKM (2016). In these studies, only a mild and not statistically significant state of hypoglycaemia and hyperuricaemia could be observed after oral consumption of 20 g/day (Seifert et al., 2008). For description of these studies, please see VKM (2016).

One additional human study was included in this revised assessment (Thompson et al., 2014): a double blind, randomised, crossover study. The participants, healthy males (N=7) and females (N=5) aged 22 to 52 years, were given single oral doses of ribose (2500, 5000 and 10 000 mg) under fasting and fed (only 10 000 mg) conditions with a wash-out period of three days between each dose. Dose-related decreases in serum glucose up to 26.3 mg/dL (1.46 mmol/L), corresponding to 30.3% of the baseline value of 86.6 mg/dL (4.81 mmol/L) at the 10 000 mg dose, occurred in the first hour post dose. For the 5000 mg dose, the mean serum glucose baseline of 85.8 mg/dL (4.77 mmol/L) was reduced to 72.6 mg/dL (4.03 mmol/L) in the first hour (observed at 30 min post dose). One of 12 participants experienced mild symptoms of hypoglycaemia 70 min post dose of 10 000 mg ribose (in the fasted state). This participant was a female weighing 53 kg. Dosing was not adjusted for bodyweight, thus, her intake dose was 188.7 mg/kg bw. The 5000 mg dose was well tolerated by all participants. A dose of 5000 mg ribose equals 94 mg/kg bw for the participant with the lowest bodyweight (53 kg).

4.2.2 Animal studies

Three animal studies on adverse health effects of D-ribose were included in the previous assessment by VKM (2016). No additional animal studies were included in this revised assessment. For description of the studies, please see VKM (2016).

4.3 Summary of hazard identification and characterisation

In the study by Thompson et al. (2014), healthy adults (N=12) were given oral single doses of ribose (2500, 5000 and 10 000 mg). Dose-related decreases in serum glucose up to 26.3 mg/dL (1.46 mmol/L), corresponding to 30.3% of the baseline value of 86.6 mg/dL (4.81 mmol/L) at the 10 000 mg dose, occurred in the first hour post dose. For the 5000 mg dose the mean serum glucose baseline of 85.8 mg/dL (4.77 mmol/L) was reduced to 72.6 mg/dL (4.03 mmol/L) in the first hour (observed at 30 min post dose). One participant experienced mild symptoms of hypoglycaemia 70 min post dose of 10 000 mg ribose. For this participant, a female participant of 53 kg, the dose equals 188.7 mg/kg bw. The 5000 mg dose was well tolerated by all participants. This dose equals 94 mg/kg bw for the participant weighing 53 kg. For all ribose doses, serum glucose levels were back to baseline 5 hours post dose.

In the previously published risk assessment (VKM, 2016), based on human studies, a dose of 20 000 mg/day of D-ribose (corresponding to 286 mg/kg bw per day in a 70 kg adult) was identified as the point of departure (POD, described as "value for comparison" in VKM, 2016) and used in the risk characterisation. The revised POD is based on the reported hypoglycaemia at a single dose of 10 000 mg D-ribose and no effects at a single dose of 5000 mg (Thompson et al., 2014). Note that the POD is not considered to be a health-based guidance value.

The revised POD is a total dose of 10 000 mg/day given as single doses of maximum 5000 mg a minimum of 5 hours apart. A single dose of 5000 mg/day corresponds to 71 mg/kg bw per day in a 70 kg adult.

5 Exposure / Intake

5.1 Food supplements

Exposure of D-ribose was estimated from the intake of food supplements. The intake of D-ribose was estimated for the age groups children (10 to <14 years), adolescents (14 to <18 years) and adults (≥18 years). The default body weights (bw) for these groups as determined by EFSA (2012) were used: 10 to <14 years: 43.4 kg; 14 to <18 years: 61.3 kg; adults (≥18 years): 70.0 kg.

From a daily dose of 3100 mg or 6200 mg of D-ribose, the intake levels are 71.4, 50.6 or 44.3 mg/kg bw per day and 142.6, 101.1 or 88.6 mg/kg bw per day for children (10 to <14 years), adolescents (14 to <18 years) and adults (≥18 years), respectively.

5.2 Other sources

The total dietary intake of D-ribose is not known. In the EU, D-ribose can be used in cosmetics as skin conditioner and humectant (CosIng, 2015).

6 Risk characterisation

In the risk characterisation, a tolerance for ribose as for adults, based on bodyweight, was assumed for children and adolescents. The risk characterisation is based on the revised POD and the estimated exposure.

- The revised POD for adults is a total dose of 10 000 mg/day given as single doses of maximum 5000 mg a minimum of 5 hours apart. A single dose of 5000 mg/day corresponds to 71 mg/kg bw per day in a 70 kg adult.
- The exposure from a single daily dose of 3100 mg and 6200 mg of D-ribose, using mean bodyweights, corresponds to 71.4 and 142.6 mg/kg bw per day for children (10 to <14 years), respectively, 50.6 and 101.1 mg/kg bw per day for adolescents (14 to <18 years), respectively, and 44.3 and 88.6 mg/kg bw per day for adults (≥18 years), respectively.

The margin of exposure (MOE) approach, *i.e.* the ratio of the POD for a single dose to the exposure, was used for the risk characterisation (Table 6-1).

Table 6-1. The calculated margins between POD for single dose (5000 mg in adults) and the exposure to ribose in food supplements for the various age groups.

Age groups (years)	Margin of exposure for a dose of 3100 mg/day	Margin of exposure for a dose of 6200 mg/day
Children (10 to <14)	1.0	0.5
Adolescents (14 to 18)	1.4	0.7
Adults (≥18)	1.6	0.8

As the MOEs for a daily dose of 6200 mg D-ribose given as a single dose are below 1.0 for children (10 to <14 years), adolescents (14 to <18 years) and adults (≥18 years), there is a risk of experiencing hypoglycaemia. Therefore, we conclude that a daily single dose of 6200 mg of D-ribose in food supplements may represent a risk of adverse health effects in these age groups.

For a daily single dose of 3100 mg D-ribose in food supplements the MOE is 1.0 for children (10 to <14 years). As the calculated exposure is based on a mean body weight for children and there were no available studies on children, we conclude that a daily single dose of 3100 mg of D-ribose in food supplements may represent a risk of adverse health effects for this age group.

For a daily single dose of D-ribose in food supplements the MOEs are 1.4 for adolescents (14 to <18 years) and 1.6 for adults (≥18 years). We conclude that it is improbable that a daily single dose of 3100 mg D-ribose in food supplements causes adverse health effects in adolescents (14 to <18 years) and adults (≥18 years).

7 Uncertainties

7.1 Uncertainty in hazard identification and characterisation

Several of the studies referred to are randomised control trials (RCTs) with relatively few participants specifically designed to investigate the positive effects of D-ribose, not potential negative effects. Some mild negative effects are reported based on self-reporting questionnaires, and also some biomarkers for physiological changes, *e.g.* blood glucose levels, were reported.

No studies on children and adolescents were identified.

A tolerance for ribose as for adults, based on bodyweight, was assumed for adolescents and children.

In the present risk assessment, potential negative nutritional effects of D-ribose were not evaluated.

7.2 Uncertainty in exposure

With use of the default (mean) body weight of an age (population) group, the variance in all individuals in the group will not be covered.

8 Conclusions with answers to the terms of reference

The Norwegian Scientific Committee for Food and Environment (VKM) has assessed the risk of D-ribose (single doses of 3100 mg/day and 6200 mg/day) in food supplements. The present risk assessment is a revision of a previous risk assessment of D-ribose (VKM, 2016).

No human studies on children (10 to <14 years) and adolescents (14 to <18 years) were identified. Therefore, a tolerance as for adults, based on bodyweight, were assumed for children and adolescents.

From a daily dose of 3100 mg or 6200 mg of D-ribose, the intake levels are 71.4, 50.6 or 44.3 mg/kg bw per day and 142.6, 101.1 or 88.6 mg/kg bw per day for for children (10 to <14 years), adolescents (14 to <18 years) and adults (≥18 years), respectively.

A mild hypoglycaemia and hyperuricaemia (changes in levels were not statistically significant) could be observed after oral consumption of 20 g/day (Seifert et al., 2008). In the study by Thompson et al. (2014), healthy adults (N=12) were given oral single doses of ribose (2500, 5000 and 10 000 mg). Dose-related decreases in serum glucose up to 26.3 mg/dL (1.46 mmol/L), corresponding to 30.3% of the baseline value of 86.6 mg/dL (4.81 mmol/L) at the 10 000 mg dose, occurred in the first hour post dose. For the 5000 mg dose the mean serum glucose baseline of 85.8 mg/dL (4.77 mmol/L) was reduced to 72.6 mg/dL (4.03 mmol/L) in the first hour (observed at 30 min post dose). One participant, a female of 53 kg, experienced mild symptoms of hypoglycaemia 70 min post dose of 10 000 mg ribose. The 5000 mg dose was well tolerated by all participants. For all ribose doses, serum glucose levels were back to baseline 5 hours post dose. The revised POD is a total dose of 10 000 mg/day given as single doses of maximum 5000 mg a minimum of 5 hours apart.

The margin of exposure (MOE) approach, i.e. the ratio of the POD for a single dose to the exposure, was used for the risk characterisation. The MOEs for a single daily dose of 3100 mg D-ribose are 1.0, 1.4 and 1.6 for children (10 to <14 years), adolescents (14 to <18 years) and adults (≥18 years), respectively. The MOEs for a daily dose of 6200 mg D-ribose given as a single dose are 0.5 for children (10 to <14 years), 0.7 for adolescents (14 to <18 years) and 0.8 for adults (≥18 years).

Conclusions

As the MOEs for a daily dose of 6200 mg D-ribose given as a single dose are below 1.0 for children (10 to <14 years), adolescents (14 to <18 years) and adults (≥18 years) there is a risk of experiencing hypoglycaemia. Therefore, we conclude that a daily single dose of 6200 mg of D-ribose in food supplements may represent a risk of adverse health effects in these age groups.

For a daily single dose of 3100 mg D-ribose in food supplements the MOE is 1.0 for children (10 to <14 years). As the calculated exposure is based on a mean bodyweight and there were no available studies on children, we conclude that a daily single dose of 3100 mg of D-ribose in food supplements may represent a risk of adverse health effects for this age group).

For a daily single dose of D-ribose in food supplements the MOEs are 1.4 for adolescents (14 to <18 years) and 1.6 for adults (≥18 years). We conclude that it is improbable that a daily single dose of 3100 mg D-ribose in food supplements causes adverse health effects in adolescents (14 to <18 years) and adults (≥18 years).

9 Data gaps

No studies on adverse health effects of D-ribose in children, adolescents, pregnant women or lactating women were identified.

There is a lack of chronic toxicity studies in animals.

Regarding potentially vulnerable groups, no studies were found that addressed pregnant and lactating women.

There is a lack of studies that have investigated the effect of high doses for longer periods than 8 weeks.

10 References

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