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Commercialisation of preparations containing *Monascus purpureus* (red mould rice, red yeast rice) is not allowed in Switzerland

Preparations containing *Monascus purpureus* (red mould rice, red yeast rice) are also encountered on the Swiss market and have given rise to debate, due to the fact that it is not clear which legislation is to be used for their assessment. As they are not authorised as medicinal products, they are frequently offered in various dosages as food supplements, either with or without therapeutic claims. While some point out that the monacolin K content of red yeast rice has a pharmacological effect typical of statins, and demand a classification as a medicinal product, others refer to the health claim for red yeast rice approved by the European Commission[1], to the assessment by EFSA[2] and to a decision of the European Court of Justice (ECJ[3]), and conclude that these preparations may be commercialised as foodstuffs.
The following article explains the reasons why preparations containing red yeast rice may neither be commercialised as medicinal products nor as foodstuffs in Switzerland at the present time, and therefore may not be placed on the market.

Initial Situation

What is Monascus purpureus or red mould rice, red yeast rice and what are its constituents?

Red mould rice is a fermentation product of conventional rice with certain strains of mould of the genus *Monascus*. The fermentation produces, in addition to red pigments, various potentially active substances such as monacolins, monankarins, ankalactones and citrinin. The relevant active substance monacolin K is identical to lovastatin, a powerful statin used as a medicinal product. Statins are pharmacologically active substances that inhibit the biosynthesis of cholesterol at the level of the hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase. The formation of the mycotoxin citrinin depends on the *Monascus* strains that are employed. Citrinin is considered to be nephrotoxic[4].
No medicinal product containing the active substance lovastatin is authorised in Switzerland. However, in some neighbouring countries, such as Germany, various authorised medicinal products comprise lovastatin. The usual initial dose is 20 mg lovastatin/day (minimum daily dosage = 10 mg).

[1] Commission Regulation (EU) No°432/2012 of 16°May2012° establishing a list of permitted health claims made on foods, other than those referring to the reduction of disease risk and to children's development and health (OJ L 136, 25.5.2012)
[2] Scientific Opinion on the substantiation of health claims related to monacolin K from red yeast rice and maintenance of normal blood LDL cholesterol concentrations (ID 1648, 1700) pursuant to Article 13(1) of Regulation (EC) No 1924/2006; EFSA Journal 2011;9(7):2304
[3] ECJ Decision No C 140/07 (online): http://curia.europa.eu/juris/document/document.jsf?text=&docid=76342&pageIndex=0&doclang=EN&mode=lst&dir=&occ=first&%20part=1&cid=1925332
[4] SKLM, German Senate Commission on the health assessment of foodstuff. Toxicological assessment of red mould rice. Update, German Research Association DGF, 2012

Recently there has been an increasing number of reports on the side effects from the use of food supplements that contain *Monascus purpureus*. It can be assumed that, with a pharmacologically active dose of monacolin K, the known and typical toxic myopathies associated with statins can also occur.

Health claims authorised by the European Commission for Monascus purpureus (red mould rice, red yeast rice)

In the EU, in accordance with Article 13 paragraph 3 of the Regulation (EU) No 1924/2006, the Commission published a European list of authorised health claims[5]. The authorisation of these claims is based on the assessment by EFSA. The list includes the following health claim for *Monascus purpureus* (red mould rice):

Nutrient, substance, food or food category	Claim	Conditions of use of the claim
Monascus purpureus (red yeast rice)	Monacolin K from red yeast rice contributes to the maintenance of normal blood cholesterol levels	The claim may be used only for food which provides a daily intake of 10 mg of monacolin K from red yeast rice. In order to bear the claim, information shall be given to the consumer that the beneficial effect is obtained with a daily intake of 10 mg of monacolin K from fermented red yeast rice preparations.

However, the evaluation by the EFSA neither represents a classification nor authorisation of *Monascus purpureus* or red yeast rice as a foodstuff, as generally the assessment of health claims does not simultaneously result in a safety assessment. A positive opinion by EFSA concerning health claims does not lead to the conclusion that the substances are safe and that products containing these substances are marketable as a foodstuff in all Member States. Recital 17 of the Regulation (EU) No 432/2012 also provides each Member State the possibility to then classify products individually as foodstuffs or medicinal products, because up to then the substance legislation had not been harmonised. The safety of monacolins from red yeast rice was recently assessed by EFSA (2018[6]).

ECJ Decision C-140/07

The ECJ had to decide whether a preparation that was placed on the market as a food supplement is possibly a medicinal product that is marketed without authorisation. The label stated as follows: *'Red Rice 330 mg, food supplement with fermented rice. One capsule corresponds to 1.33 mg of monacolin K'. The recommendations for use are: As food supplement, 1 capsule 1 - 3 times daily'.* The decisive factor was that the recommended dose amounts to a daily consumption of 1.33 to 4 mg of monacolin K, which is low in comparison with the daily consumption of 10 to 80 mg recommended for the authorised, prescription-based lovastatin.

The ECJ held that products containing a substance having a physiological effect cannot automatically be classified as medicinal products by function unless the competent authorities have made an assessment, with due diligence, of each product. A product

[5] Commission Regulation (EU) No°432/2012 of 16°May2012 establishing a list of permitted health claims made on foods, other than those referring to the reduction of disease risk and to children's development and health (OJ L 136, 25.5.2012)
[6] Scientific opinion on the safety of monacolins in red yeast rice, EFSA Journal 2018; 16(8):5368

cannot be regarded as a medicinal product by function where, having regard to its composition and dosage – and if used as intended, it is incapable of appreciably restoring, correcting or modifying physiological functions. In the present case the dosage was too low to classify the preparation as a medicinal product by function.

Conclusions: Many red mould rice preparations, imported from abroad as food supplements and intended to be placed on the market in Switzerland, contain significantly less than 10 mg monacolin K and therefore must not be advertised with the mentioned health claims – even abroad.

Assessment of the safety of monacolins from red yeast rice by EFSA[7]

The safety of using monacolins in food supplements was recently assessed by EFSA on behalf of the European Commission. In its assessment, EFSA could not determine a safe daily dosage of monacolin K in food supplements. It concluded that consuming monacolins from red yeast rice via food supplements could lead to an estimated intake of monacolin K that is similar to the therapeutic dose of lovastatin. On the basis of the information available about red yeast rice and its undesirable effects on humans on the musculoskeletal system (including rhabdomyolysis) and on the liver, EFSA came to the conclusion that taking 10 mg of monacolins per day from red yeast rice as a food supplement presents significant safety concerns. The panel considered that individual cases of severe adverse reactions have been reported for monacolins from red yeast rice at intake levels as low as 3 mg per day.

Is the placing on the market as a foodstuff possible in Switzerland?

In Switzerland the placing on the market of preparations containing red mould rice as foodstuffs is not possible for the following reasons:

- Those preparations that contain an effective dose of monacolin K produce their effect through a pharmacological mode of action (identical to that of statins) and in accordance to the delimitation criteria of the Federal Supreme Court are not subject to the food legislation.
- Foodstuffs, when consumed normally, must not endanger health. In this case there are significant doubts in regard to their safety. Monacolins are potent pharmaceutical substances to reduce cholesterol and may only be administered under medical supervision. Products containing monacolin K are considered to be unsafe foodstuffs, due to the generally missing standardised monacolin content, to the danger of undesirable effects of monacolin K, to the lack of medical control of the consumption, as well as to the additional toxicologically questionable constituents. In this context, reference is made to the evaluation of the EFSA, the findings of the German Research Association, the Senate Commission on the health assessment of foodstuffs (SKLM[8]) and the opinion of the German joint Expert Commission BVL/BfArM, 'Classification of red mould rice products' (02/2016)[9]. Questions on safety are particularly those in regard to the muscle toxicity of monacolin K and the nephrotoxicity of citrinin. Specifications to ensure purity and identity of the preparation as well as data on the absence of toxic constituents are missing.
- Consequently, with the totally revised foodstuff legislation that entered into force

[7] Scientific opinion on the safety of monacolins in red yeast rice, EFSA Journal 2018; 16(8):5368
[8] SKLM, German Senate Commission on the health assessment of foodstuffs (2012). Toxicological assessment of red mould rice. Update, final edition of 18.12.2012
[9] Opinion of the German joint Expert Commission BVL/BfArM. Classification of red mould rice products (02/2016)

on 1 May 2017, *Monascus purpureus* was included in the list of substances that may not be added to foodstuffs in Switzerland (Annex 4 of the FDHA Ordinance on the Addition of Vitamins, Minerals and other Substances to Foodstuffs; AVMO; SR 817.022.32) and thus is not marketable as a foodstuff.

- Therefore, food supplements containing *Monascus purpureus* may not be placed on the market in Switzerland, as Annex 4 AVMO in accordance with Art. 2 para. 4 of the Ordinance on Food Supplements (SR 817.022.14), also applies to food supplements.

Is the placing on the market as a formulated medicinal product possible?

It was recently observed that sporadic attempts have indeed been made to circumvent the marketing prohibition as a foodstuff or the need for authorisation as a medicinal product by selling or prescribing these preparations as e.g. a formula magistralis/propriety formula.
According to the Swiss legislation on therapeutic products this practice is not possible for the following reasons: The Medicinal Products Ordinance (SR 812. 212. 21) specifies in Art. 37 those active principles that may be used in formulated medicinal products. Red yeast rice containing various pharmacologically active monacolins is not included in any authorised medicinal product and does not comply with the conditions listed in the Ordinance. Consequently, it cannot be used as an active principle for the preparation of formulated medicinal products.

Conclusions

At present in Switzerland, *Monascus purpureus* (red mould rice, red yeast rice) is neither authorised as a medicinal product nor as a foodstuff. Therefore it may not be marketed.