cvua Karlsruhe

Chemisches und Veterinär-untersuchungsamt Karlsruhe

Ozempic® - the diabetes injection that is also used as a "slimming product"

Suspected falsification now also confirmed analytically

The Drugs, Cosmetics and NMR departments of the CVUA Karlsruhe

Ozempic® is a medicinal product authorised for the treatment of diabetes. However, because it also suppresses the appetite, celebrities claim Ozempic® as a "slimming injection". Since October, authorities from several countries have issued warnings concerning dangerous falsified versions of the drug. Through analytical testing, the CVUA Karlsruhe has now determined that suspected Ozempic® pre-filled pens contain the drug insulin glulisine instead of the claimed active substance, semaglutide. Use of the falsified Ozempic® syringes containing insulin by people who do not have diabetes can lead to dangerous hypoglycaemia with cramps and sudden loss of consciousness.

Isolated Ozempic® batches are currently suspected of being fake. The falsified medicinal products have attracted attention because of a significant difference in the appearance of the original Ozempic® pre-filled syringes and that of the falsified pre-filled pens (press release from the Freiburg Regional Council). In addition, a number of people in Austria who used these suspected pre-filled syringes were admitted to hospital with typical symptoms of low blood sugar (hypoglycaemia). These falsified products pose a considerable health risk!

Due to the similarity of their appearance to the Apidra® Solostar insulin pen, it was suspected that the falsified products could be re-labelled insulin pens.

Fig.1: Ozempic® falsified pen, Apidra® ready-to-use pen, Ozempic® ready-to-use pen

Using liquid chromatography coupled with high-resolution mass spectrometry (LC-HRMS) and nuclear magnetic resonance spectroscopy (NMR), the Chemical and Veterinary Investigation Office in Karlsruhe has been able to demonstrate that the injection solution in the suspected falsified pre-filled syringes contained the active substance insulin glulisine and not semaglutide, the active substance in Ozempic®.

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Active substances insulin glulisine and semaglutide

Insulin glulisine (Apidra®)

Insulin regulates the uptake of glucose into the body's cells through its blood sugar-lowering effect. Insulin glulisine is a fast-acting insulin with a shorter duration of action. Fast-acting insulins can cause acute hypoglycaemia and severe dosing errors can lead to a life-threatening coma, as the body no longer has any sugar available for cell metabolism.

Semaglutide (Ozempic®)

Semaglutide is a slow-acting and indirect blood glucose-lowering agent. It increases the release of insulin by binding to certain receptors, thus lowering blood glucose levels.

It was possible to differentiate between the active substances through chromatographic separation coupled with determination of their exact masses and the distribution of the different natural atom types of the elements they contain (isotope distribution).

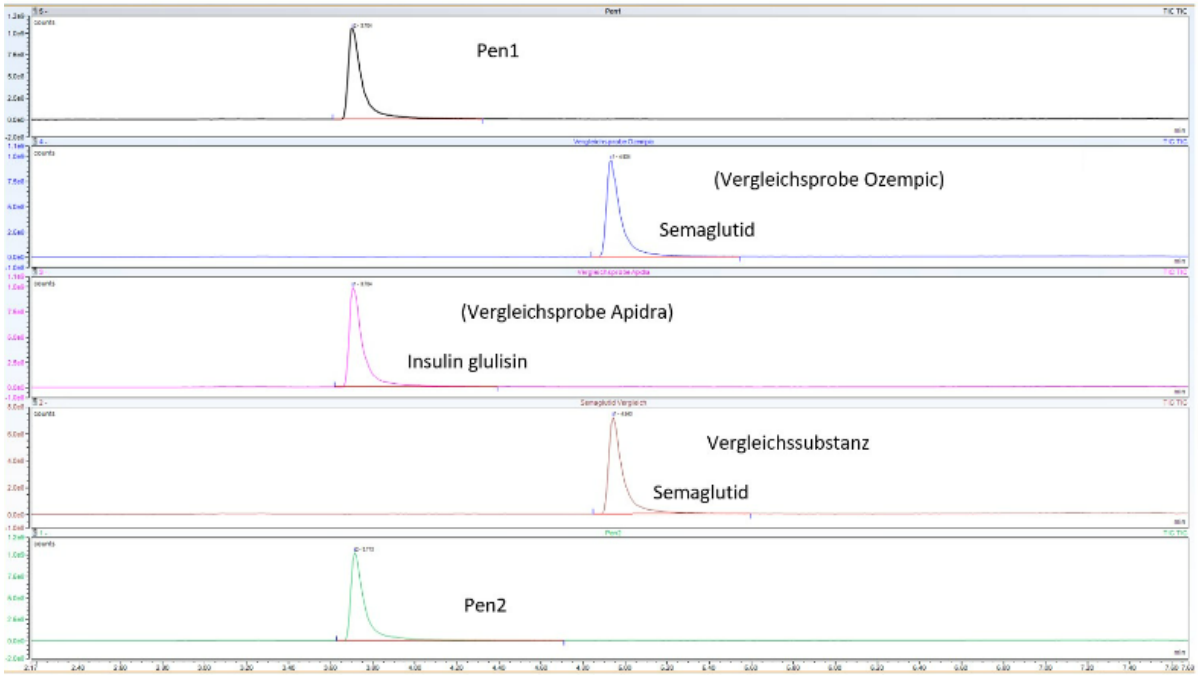

Fig.2: Chromatograms of Ozempic® falsified pens 1 and 2, semaglutide from the real Ozempic®, Apidra® with insulin glulisine

Info box

LC-HRMS analysis technique

LC-HRMS stands for liquid chromatography coupled with high-resolution mass spectrometry. Using this technique, after chromatographic pre-separation of the substances to be determined, the exact mass-to-charge ratio of ions can be determined with high mass resolution and mass accuracy. The data thus obtained can be used to precisely determine the chemical composition of substances. Tandem mass spectrometry, i.e. fragmentation of the substances followed by mass spectrometry, can be used to further clarify the structure of a substance.

Proton nuclear magnetic resonance spectroscopy (^{1}H-NMR spectroscopy) also confirmed that the composition of the suspected injection solutions did not match that of Ozempic®, but was very similar to that of the insulin preparation Apidra® Solostar (see Figures 3 and 4). In addition to the active substances, the medicinal products can also be distinguished on the basis of the excipients (stabilisers) they contain. Cresol and trometamol, excipients in Apidra® Solostar, were detected in the suspected samples in comparable quantities to those found in Apidra® Solostar medicinal product (see Figure 3). Ozempic® does not contain these excipients. Furthermore, the excipients phenol and propylene glycol, both included in Ozempic®, were not identified in the suspected sample. Polypeptide fingerprinting also found no match between the suspected sample and a sample of authentic Ozempic® (see Figure 4).

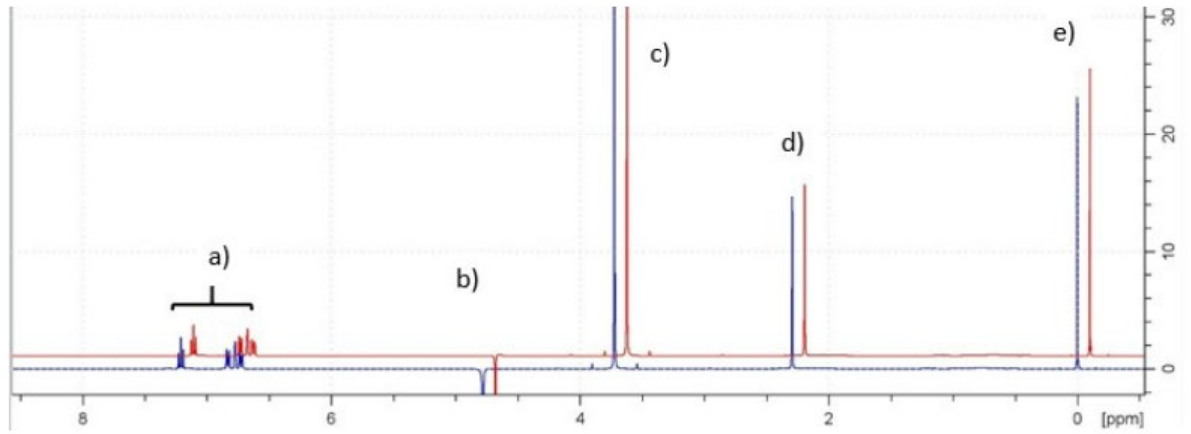

Fig.3: ^{1}H-NMR signals of the excipients of falsified (red) and real Apidra® (blue) show very good correlation. a) Signals from cresol b) Residual signal from water c) Signal from trometamol d) Signal from cresol e) Signal from the internal standard

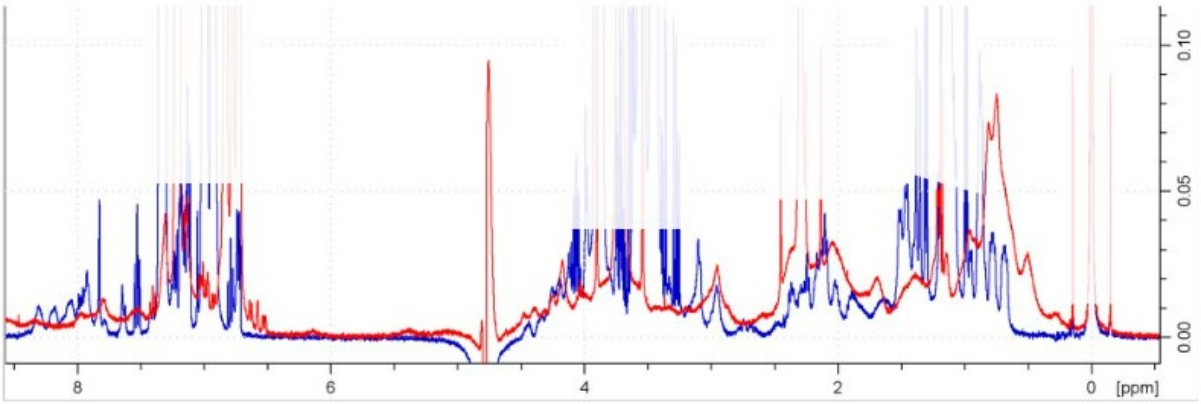

Fig.4: ^{1}H-NMR spectra of falsified (red) and real Ozempic® (blue), strongly vertically zoomed and intense signals attenuated to visualise the background of weak signals of the polypeptides - no agreement of the spectra

Info box

NMR analysis

NMR spectroscopy (Nuclear Magnetic Resonance) is an analytical method that can be used to identify substances and determine their concentrations. Some atomic nuclei (e.g. hydrogen, ^{1}H) show distinct magnetic properties when they are placed in a strong magnetic field. These atomic nuclei can then be excited and subsequently emit characteristic signals. The frequency and shape of these signals depend on the electronic environment of the atomic nuclei. Molecular structure therefore has a characteristic influence on the NMR spectrum and can often be deduced from it. The intensity of the signals provides information about the concentration of the substance(s) in the sample. NMR spectroscopy is one of the most powerful methods for identifying and characterising the structure of compounds and a primary method for determining concentration. Proton NMR spectroscopy (^{1}H-NMR) is used most frequently.

Conclusion

The use of falsified Ozempic® pens can have life-threatening consequences for patients. Therefore, only products obtained on prescription via legal distribution channels should be used. If you suspect that an Ozempic® pen is falsified , please contact a pharmacy. They can check the authenticity of the medicine. The CVUA Karlsruhe will continue to investigate suspicious products in order to protect patients from falsified medicines.

Further information can be found on the homepage of the Federal Institute for Drugs and Medical Devices (BfArM - Falsification of the drug Ozempic®).

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An information service of the German Chemical and Veterinary Investigation Offices (CVUA) Stuttgart, Karlsruhe, Freiburg and Sigmaringen and the State Veterinary Investigation Office (STUA) Aulendorf - Diagnostic Centre.