The calcium-channel blocker diltiazem is a highly unstable drug in blood and is rapidly converted by chemical and enzymatic processes to deacetyldiltiazem (even in fluoride containers). Therefore, the measurement of diltiazem alone may not be a true reflection of the concentration immediately after death or sample collection. This protocol describes a means of determining the concentration of diltiazem and deacetyldiltiazem in blood to evaluate the possible degree of in vitro instability with resultant implications for the interpretation. Deacetyldiltiazem is also a pharmacologically active metabolite.

The literature indicates therapeutic diltiazem concentrations are typically <0.3 mg/L in life plasma, with levels usually >1 mg/L and >6 mg/L associated with overdosage and death, respectively. However, in such cases there was not always measurement/estimation of the plasma, with levels usually >1 mg/L and >6 mg/L associated with overdosage and death. The measurement of diltiazem alone may not be a true reflection of the concentration immediately after death or sample collection. This protocol describes a means of determining the concentration of diltiazem and deacetyldiltiazem in blood to evaluate the possible degree of in vitro instability with resultant implications for the interpretation. Deacetyldiltiazem is also a pharmacologically active metabolite.

The objective of this study was to aid the interpretation of cases involving diltiazem by determining the concentration of diltiazem and its metabolite/breakdown product deacetyldiltiazem (deacetyldiltiazem).

**Introduction**

Deacetyldiltiazem standards produced from fresh diltiazem plasma standards that are allowed to degrade. Standards and QCs are then frozen at -20°C. Continuous instability and conversion of the diltiazem still occurs at -20°C.

2. Fresh diltiazem plasma standard prepared and rapidly serially diluted to measure diltiazem and deacetyldiltiazem concentration is lower than 6 mg/L.

3. Deacetyldiltiazem concentration calculated by subtracting the current diltiazem concentration (e.g. 8.2 mg/L) of the frozen standards from the original concentration (e.g. 10 mg/L). In this example producing a deacetyldiltiazem concentration of 0.8 mg/L.

4. Resultant deacetyldiltiazem concentrations of original frozen standards used as calibrants to measure the deacetyldiltiazem concentration in the QCs and the case sample(s).

5. Methodology controlled by the analysis of QCs (1 mg/L and 5 mg/L). For example, addition of the current diltiazem concentration (e.g. 3.7 mg/L) and the deacetyldiltiazem concentration (e.g. 1.3 mg/L) based on the separate calibration curves should be equivalent to the starting concentration (in this example, 5 mg/L).

**Methodology (1)**

Deacetyldiltiazem standards produced from fresh diltiazem plasma standards that are allowed to degrade. Standards and QCs are then frozen at -20°C. Continuous instability with resultant implications for the interpretation. Deacetyldiltiazem is also a pharmacologically active metabolite.

**Methodology (2)**

1. Deacetyldiltiazem standards produced from fresh diltiazem plasma standards that are allowed to degrade. Standards and QCs are then frozen at -20°C. Continuous instability and conversion of the diltiazem still occurs at -20°C.

2. Fresh diltiazem plasma standard prepared and rapidly serially diluted to measure diltiazem content in the QCs, frozen (deacetyldiltiazem standards and the case sample(s). This determines the current diltiazem concentration.

3. Deacetyldiltiazem concentration calculated by subtracting the current diltiazem concentration (e.g. 8.2 mg/L) of the frozen standards from the original concentration (e.g. 10 mg/L). In this example producing a deacetyldiltiazem concentration of 0.8 mg/L.

4. Resultant deacetyldiltiazem concentrations of original frozen standards used as calibrants to measure the deacetyldiltiazem concentration in the QCs and the case sample(s).

5. Methodology controlled by the analysis of QCs (1 mg/L and 5 mg/L). For example, addition of the current diltiazem concentration (e.g. 3.7 mg/L) and the deacetyldiltiazem concentration (e.g. 1.3 mg/L) based on the separate calibration curves should be equivalent to the starting concentration (in this example, 5 mg/L).

**Results**

**Conclusions**

The method has enabled the measurement of diltiazem and deacetyldiltiazem in case samples. Although diltiazem overdosage is uncommon it has been a useful aid in evaluating the toxicological significance if suspected. It is strongly recommended that laboratories consider the concentrations of both diltiazem and deacetyldiltiazem when investigating such cases.

**References**


