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# A Short Note on Lacosamide and its Main Metabolite Combined Pharmacokinetic Model

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## Introduction

The integration of data to determine the proper dosage selection and dosing regimens, which are essential components of clinical drug development, is made possible by pharmacokinetic (PK) modelling and simulation [1,2]. To convert drug dosage into concentrations that may be employed in customised therapy regimens, a PK model that takes into account unique patient characteristics and is based on the study of concentration-time data is required [3]. A knowledge of dose-related adverse events (such as toxic consequences) and information on the effective concentrations in plasma are provided by the development of the mathematical context of a drug concentration in various tissues and bodily fluids [4]. It's important to create new models that take into account the model-dependent PKs of a drug and its metabolites in plasma and of the unchanged drug in urine. Although many PK text books describe the model-dependent PK of a drug in a tissue (e.g., drug in plasma or excreted in urine) to reflect the complex mechanisms of transport processes. The PK profile of a medication and its metabolites might change due to a number of physiological and pathological events, including impaired renal or hepatic function, necessitating modifications to conventional dosage regimens [5]. It may be possible to determine the pertinent PK parameters from given concentrations in plasma and quantities in urine with the construction of a PK model that precisely depicts the kinetics of a medication and its metabolites through the body, including the quantity excreted in urine. Due to the overlap of some PK parameters among the three models (i.e., PKs of the drug and metabolite in plasma and drug excreted in urine), PK parameters act as the link between them. Understanding diverse drug concentration-time curves in plasma and drug exposures in patients with various medical conditions, such as renal impairment, might benefit from making use of this link.

We use lacosamide, a more recent antiepileptic drug (AED) that has been approved (in doses up to 400 mg/day) for the treatment of focal seizures in adults as monotherapy (US only) or adjunctive therapy (US, EU, and other countries) [6,7]. It selectively enhances the slow inactivation of voltage-gated sodium channels. Lacosamide has been shown to be effective and safe as an additional treatment [8-10] as well as when converted to lacosamide monotherapy [11] in adults with partial-onset seizures. In certain adult patients with partial onset seizures who had been seizure-free after lacosamide add-on medication, a 1-year prospective trial that reflected clinical practise revealed that conversion to lacosamide monotherapy might be efficacious and well tolerated [12]. Lacosamide had no first pass effect and dose-proportional PKs following oral administration of a single dosage (100–800 mg). The terminal half-life is around 13 hours, and plasma protein binding is less than 15%. After the start of the dosage, steady-state plasma levels can be reached in 3 days [13]. Lacosamide is mostly eliminated via the kidneys (95%), with the other metabolites accounting for the remaining 40% of the lacosamide that is not completely metabolised. The volume of distribution, Vd, is 0.6 L/kg and is almost equal to the amount of water in the entire body [14,15]. Lacosamide also has no interactions with popular AEDs. An acceptable PK model that can simulate and anticipate different case situations, fit lacosamide data, and fit the data, might offer a better knowledge of how the drug behaves in certain patients. Additionally, relevant mathematical models should help to clarify the connection between the parent drug's PK characteristics and its metabolism and excretion. The lacosamide model may serve as a foundation for PK modelling with different medications. By iterating the values for the PK parameter based on the models, the software's eligibility for PK modelling was verified. Statistics were used to analyse the outcomes of validation. The appropriateness of the created system of PK models was further assessed using data from the lacosamide trial in both healthy and renally impaired participants.

## Conclusion

A novel combined PK model has been developed, and it represents the model-dependent PK of the drug's unmodified form in plasma and urine as well as its metabolite in plasma. Additionally, the PK model was used to determine the plasma concentrations of lacosamide, its primary metabolite, and the quantities of lacosamide excreted in urine in both healthy and patient populations with mild to severe renal impairment during a Phase I study. The PK parameters were consistent with how we currently understand the drug's behaviour in this population and help us better understand how renal function affects the renal excretion of lacosamide and its main metabolite as well as how renal function and lacosamide's metabolism are independent of one another.

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Not applicable.

## Conflict of Interest

Author declares no conflict of interest.

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