# Reassessing Pharmacokinetics in Plant Extracts: A Case Study of Oleandrin and Its Hydroalcoholic Extract

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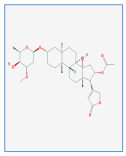
## INTRODUCTION AND OBJECTIVE

Preclinical toxicology, essential for drug registration, provides some measure of potential human risk. Due to complex composition, it's crucial to assess plant extract pharmacokinetics when therapeutically relevant, as active compound pharmacokinetics may differ.
Oleandrin, the active and toxic compound of *Nerium oleander L* has garnered significant interest in recent years due to its anti-tumor and anti-viral properties.

**Aim**

The objective of this work is to illustrate the necessity of reassessing pharmacokinetics depending on the plant extracts, using the pharmacokinetics of oleandrin in the alcoholic extract of Nerium oleander, compared to published data on its pharmacokinetics when administered in its pure form.



Chemical structure of Oleandrin

## METHODS

| EXPERIEMENT | VS | LITERATURE[3] |
|---|---|---|
| MIXTURE | | ISOLATED COMPOUND |

- A hydroalcoholic extract was used : *Nerium oleander* leaves underwent a process involving powdering, maceration in 70% ethanol, filtration, rotary evaporation and lyophilization.
- Pharmacokinetic studies of oleandrin were conducted in Swiss male mice after administering both intravenous (I.V.) and oral (P.O.) doses of a hydroalcoholic extract of Nerium oleander.
- For oral studies, a dose of 150 mg/g was administered (equivalent dose of 1710 µg/kg) via gastric feeding, with seven sampling times at 10, 20, 30, 40, 60, 120 and 180 min.
- Intravenous studies involved a dose of 30 mg/g (equivalent dose of 342 µg/kg) administered through injection, with sampling times at 10, 30, 60, and 120 minutes.
- Excretion studies utilized seven mice, administered a dose of 150 mg/g, with urine samples collected at 48 hours.
- Sample preparation involved mixing samples with a deuterated standard solution and acetonitrile, followed by LC-MS/MS analysis.
- Pharmacokinetic parameters were calculated using PK Solver 2.0 software.

- $^{3}$H oleandrin was used.
- Pharmacokinetic studies were conducted in male CD1-mice after administering both intravenous (I.V.) and oral (P.O.) doses of $^{3}$H oleandrin.
- Intravenous (IV) administration involved a dose of 40 µg/kg, while oral studies utilized a dose of 80 µg/kg.
- Excretion used a dose of 40 µg/kg, with urine samples collected at 0, 4, 7, 24 and 48 hours.
- LC-MS/MS was employed for oleandrin quantification.
- Pharmacokinetic parameters were calculated using WinNonlin 3.1.

## RESULTS AND DISCUSSION

- Cmax at 10 min.
- Bioavailability of 61.6 %.
- The apparent volume of distribution Vss was 0.55 L/kg.
- Clearance ClT was 0.01 kg* L/min.
- Oleandrin in urine represents 0.986% of the initial dose administred.

- Cmax at 20 min.
- Bioavailability of 29.3 %.
- The apparent volume of distribution Vss was 0.3±0.2 L/kg.
- Clearance ClT was 1.13±0.41 L/h.kg.
- Oleandrin in urine represents 1.9 % of the injected dose.

Oleandrin in the extract has been absorbed faster (Tmax 10 min vs. 20 min alone).
Extract bioavailability (61%) is double that of oleandrin alone (30%), likely due to absorption-enhancing substances, possibly P-glycoprotein inhibitors.

## CONCLUSION

In conclusion, this study highlights the importance of reevaluating pharmacokinetics when working with plant extracts. Specifically, distinct pharmacokinetic profiles for oleandrin in its pure form versus an hydroalcoholic extract of *Nerium oleander* were observed. These findings underscore the complexity of plant extract pharmacokinetics, emphasizing the need for thorough assessments in herbal research.

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