

## Reviewer's report

**Title:** Diclofenac does not interact with codeine metabolism in vivo: A study in healthy volunteers

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**Reviewer:** Jurgen Drewe

**Level of interest:** A paper whose findings are important to those with closely related research interests

**Advice on publication:** Accept after discretionary revisions

Ammon et al. show in their paper that in contrast to in vitro experiments diclofenac did not alter glucuronidation of codeine in vivo. The authors demonstrated that in vivo no evidence of an interaction with diclofenac could be found. The methods of the study are adequate. The results are relevant and clearly supporting the author's conclusion.

However, there are some minor points.

1. It would have been nice to have a chart of the metabolic pathways, which make it easier for the reader to judge the importance of the effects
2. Did the PK data differ for the intermediate metaboliser ?
3. There was no placebo administration in the study. Were dynamic measurements statistically analysed for period effects to account for possible habituation effects over time ?
4. Page 9, Pharmacokinetic evaluation:  $\lambda_{dz}$  was not explained. How was it assessed? Give more details of non-linear regression.

### Competing interests:

None declared.