

# Antiprion drugs 6-aminophenanthridine and guanabenz reduce PABPN1 toxicity and aggregation in oculopharyngeal muscular dystrophy

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## Supplementary Material

### Supplementary Figure legends

**Supplementary Figure 1:** Toxicity and effect of candidate drugs on the *Drosophila* model of OPMD. Toxicity was determined using wild-type individuals fed with the drugs from first instar larval stage (n=110 to 120). To analyse the effects of the drugs, OPMD (*UAS-PABPN1-17ala/+; Mhc-Gal4/+*) individuals were raised at 18°C on drug-supplemented medium from first instar larval stage. Adult males were transferred onto fresh medium with the same concentration of drug, wing position was scored at day 6 (n=134 to 198). None of these drugs is active in the *Drosophila* model of OPMD. The differential effects of trehalose in the mouse and *Drosophila* models of OPMD could result from the very different metabolism of this compound in mammals and insects (Liebl et al, 2010). Concerning doxycycline, a high concentration was used to reveal a beneficial effect in the OPMD mouse model (6 mg/ml (Davies et al, 2005)). Because doxycycline is toxic (Smith et al, 2003) (A), it is likely that the highest concentration we could use in *Drosophila* was too low to observe a potential beneficial effect.

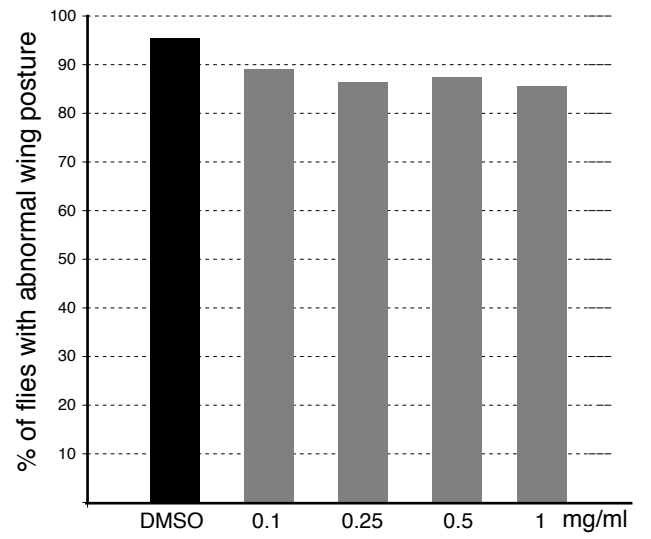
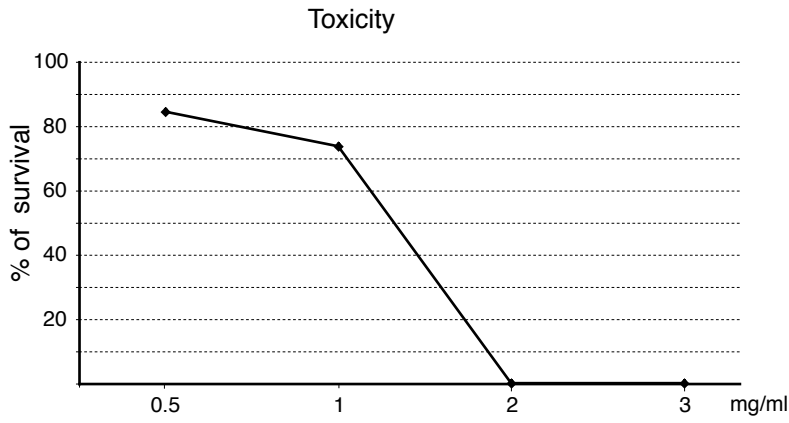
**Supplementary Figure 2:** Toxicity of 6AP and 6APi fed to OPMD larvae at 18°C. Toxicity of the drugs was determined by transferring 80 OPMD (*UAS-PABPN1-17ala/+; Mhc-Gal4/+*) first instar larvae into vials containing 5 ml of instant *Drosophila* medium reconstituted with increasing concentrations of drug in DMSO. The graph shows the percentage of flies reaching adulthood (n=320 per condition). The percentage of survival of OPMD larvae raised on DMSO alone at the highest concentration (0.6%) was 80% (n=320). Despite their muscle defects, OPMD larvae were able to feed and their survival rate was very low in the presence of 600 mM of 6AP, as it was the case for wild-type larvae.

**Supplementary Figure 3:** Beneficial effect of 6AP when provided to larval stages only or from late larval to adult stages. *UAS-PABPN1-17ala/+; Mhc-Gal4/+* larvae were raised at 18°C on instant *Drosophila* medium supplemented with DMSO alone or 400 µM of 6AP. Individuals were fed with the drug from either first instar larval to adult stages (Larval+Adult), first instar to third instar larval stages (Larval only), or third instar larval to adult stages (Late Larval+Adult). Wing position defects were scored at day 6 (n=45 to 153). \*\*\* *P*-value <10<sup>-3</sup> using the  $\chi^2$  test.

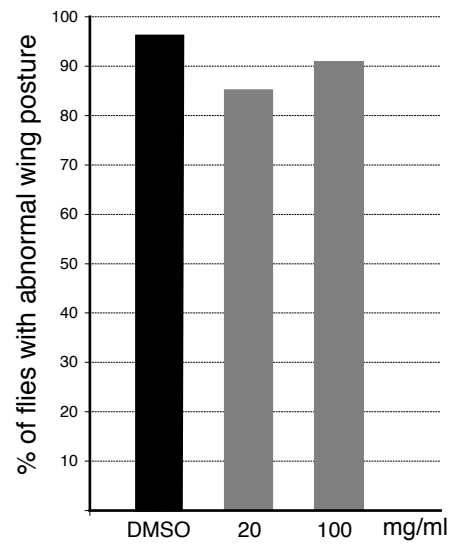
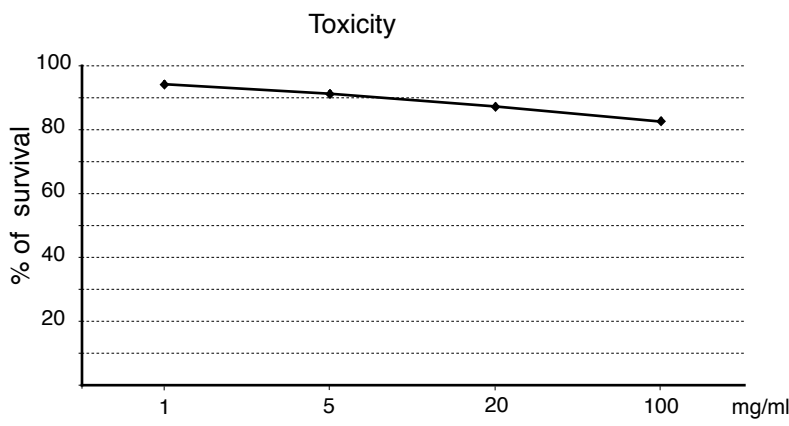
### References

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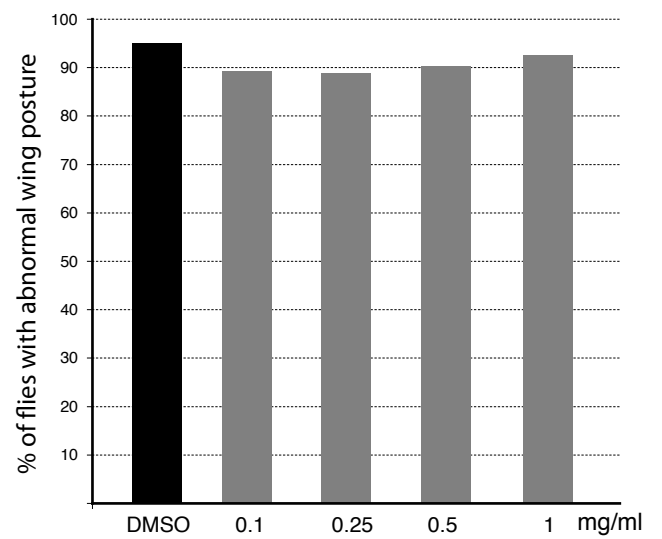
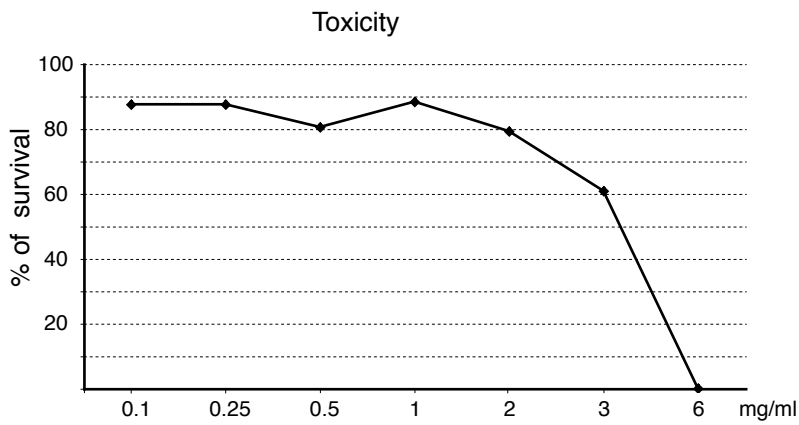
A Doxycycline



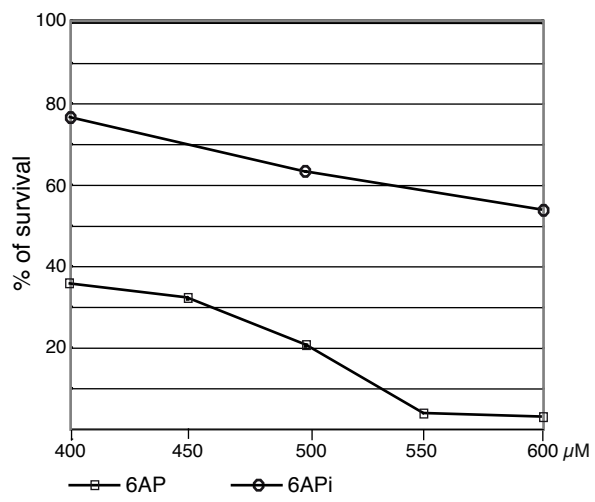
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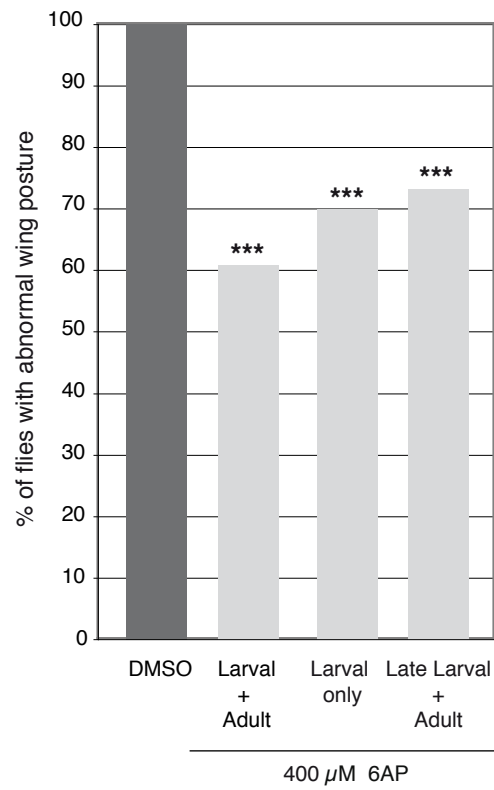
C Ibuprofen



Supplementary Figure 1



Supplementary Figure 2



Supplementary Figure 3