Interactions between enrofloxacin and fipronil in vitro study

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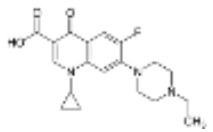
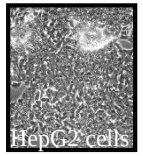
Particular public attention is focused on the presence of veterinary drugs in the food of animal origin and in the environment. The presence of these chemotherapeutic agents in varying concentrations can pose a serious problem in human exposure to these drugs. There are more and more opinions in the literature that interactions among veterinary drugs especially between enrofloxacin and fipronil are unrecognized problem in veterinary toxicology. The problem is exacerbated by the lack of data on human exposure to a mixture of these veterinary drugs present in food and the ecosystem. Enrofloxacin is the most commonly used antimicrobial veterinary drug in Poland. Fipronil is registered as veterinary medicine and is most commonly used to control ectoparasites in companion animals. The concentrations of both veterinary drugs are detected in food, environment, and plants.

The aim of the study was verify the occurrence of cytotoxic interactions between two veterinary drugs: enrofloxacin and fipronil in humans.

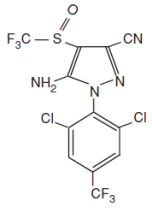
Materials and methods

Enrofloxacin





Fipronil



72 h

MTT assay (cellular metabolism)
TPC assay (total protein content)
NRU assay (lysosomal activity)
LDH assay (integrity of cellular membrane)

EC_{20}

Combination Index – CI

≤0.9 - synergism

>0.9 and <1.1 - additive effect

≥1.1 - antagonism

Conclusion

Mixtures of study veterinary drugs show higher cytotoxicity than the effects of individual drugs.

Their character of interaction between this drugs is strong synergistic. This can lead to many health complications for consumers

The presented research was performed in the frame of the project funded by the National Veterinary Research Institute in Pulawy as part of the own research project "Interactions of veterinary drugs in vitro study,,.

Results

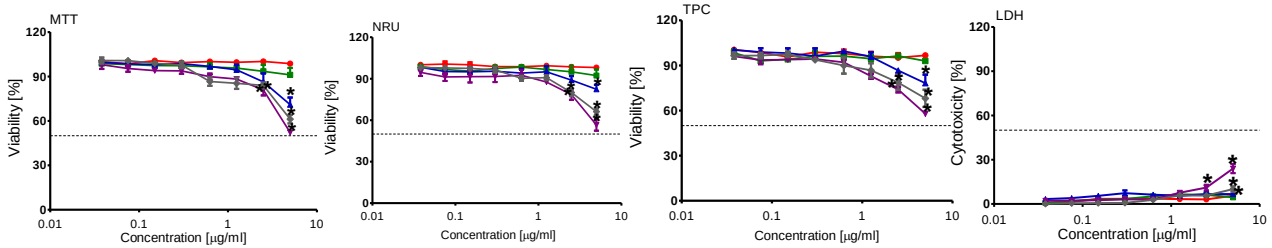


Fig.1. The effects of enrofloxacina and fipronil alone (0.04-5 µg/ml) and mixtures this drugs (1:1; 1:2 and 2:1) on human (HepG2) hepatoma cells. The values are expressed as means ± SD (n=3), (*P ≤0.05)

Table 1. Values of the EC20 of enrofloxacin and fipronil and mixtures these drugs were measured in incubates of HepG2 cell cultures.

Method	ENRO	FIPR	Mixture - ENRO+FIPR		
			1:1	1:2	2:1
MTT	>5	>5	3.3±0.4	2.8±0.8	3.1±0.6
NRU	>5	>5	>5	2.3±0.2	2.5±0.1
TPC	>5	>5	4.5±0.4	1.6±0.2	2.4±0.1
LDH	>5	>5	>5	4.3±0.7	>5

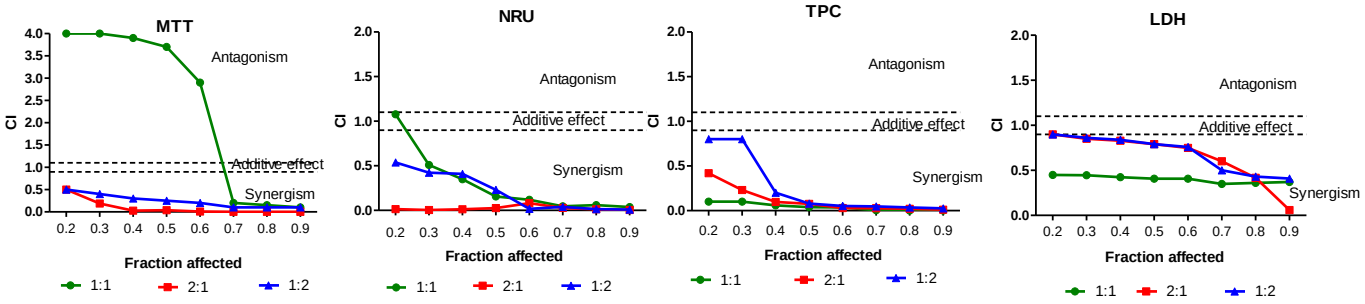


Fig.2. Combination index-fraction affected curves (CI-Plot) for the combination of ENRO and FIPR in three combinations in HepG2 at 4 different assays. The vertical bars indicate 95% confidence intervals for CI values based on sequential deletion analysis. Horizontal dashed lines indicate the additive level, which separates synergism and antagonism side.