# OBTAINING OF A VIRAZOLE-RESISTANT FOWL PLAGUE VIRUS MUTANT

*M. K. Indulen, R. L. Feldblum*

The A. Kirchenstein Institute of Microbiology, Academy of Sciences of the Latvian S.S.R., 226067 Riga, U.S.S.R.

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Rimantadine-resistant variants were easily obtained with both fowl plague (FPV) and human influenza A/Krasnodar/ 101/59 (H2N2) viruses (*1*, *2*). On the other hand, no Virazole-resistant clones were found in influenza A and B virus populations (*3*).

We examined the possibility of obtaining a Virazole-resistant FPV variant. We used Virazole and rimantadine synthesized in the Institute of Organic Synthesis, Academy of Sciences of the Latvian S.S.R.

FPV strain Weybridge (Hav1Neq1) was passaged in chick embryo cell (CEC) cultures in the presence of increasing drug concentrations (10-50 μg/ml) in medium 199. The cultures were infected at a multiplicity of 1 PFU per cell and incubated for 20 hr at 37° C. In parallel controls, the virus was passaged in the absence of drug. The sensitivity of the viruses to Virazole and rimantadine was assayed by plaque titration in the presence and absence of the drug at an input of 100 PFU per cell monolayer. The inhibition of plaque formation was expressed in per cent of control of the corresponding virus incubated in the absence of the drug.

Virazole in concentrations of 12.5 and 25 μg/ml reduced the number of FPV plaques by 89 and 93%. The concentration of 25 μg/ml was then used in all further experiments.

In the course of 8 passages in the presence of 10-50 μg/ml Virazole, the sensitivity of FPV to the drug decreased 3-fold as compared with control virus:

Inhibition of plaque formation (%) by 25 μg/ml Virazole at CEC passage level

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|---|---|
| FPV (control) | 93 | 95 | 91 | 90 | 95 | 93 | 93 | 92 |
| FPV + Virazole | 90 | 70 | 69 | 68 | 68 | 55 | 40 | 30 |

From the population of the 8th passage we isolated a Virazole-resistant mutant of FPV ($FPV_{VR}$) by cloning from a large plaque formed in the presence of 25 μg/ml Virazole.

This Virazole-resistant mutant ($FPV_{VR}$) had a somewhat lowered sensitivity to rimantadine. Inhibition of plaque formation on inoculation of 100 PFU per cell monolayer in the presence of 25 μg/ml of either drug reached 93% (FPV) and 10% ($FPV_{VR}$) with Virazole and 95% (FPV) and 80% ($FPV_{VR}$) with rimantadine. The rimantadine-resistant mutant of FPV, obtained in previous experiments, showed a lower sensitivity to Virazole (*1*).

## References

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