

1 **EVALUATION OF RETINAL PERMEABILITY OF METHOTREXATE FOR**
2 **THERAPEUTIC TREATMENT OF INTRAOCULAR LYMPHOMA**

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1 **ABSTRACT:**

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3 **Purpose:** Intraocular Lymphoma (IOL) provides a therapeutic challenge because of its diverse
4 clinical picture and aggressive course. Our objective was to evaluate the retinal permeability (RP)
5 of Methotrexate (MTX) and investigate its intravitreal pharmacokinetics in the human eye
6 following an intravitreal injection and a controlled release implant to determine the therapeutic
7 treatment protocol for IOL.

8 **Methodology:** The 3-D eye model of rabbit was adapted from our previous studies and a human
9 eye model was constructed based on the physiological dimensions. The RP of MTX was the
10 unknown parameter in the model and was determined by comparing the model simulated vitreous
11 concentrations with the available *in vivo* data.

12 **Results:** The RP values of MTX calculated for an albino rabbit and human eye were 9.25×10^{-6}
13 cm/s and 9.09×10^{-6} cm/s respectively. We have simulated and investigated the existing Induction–
14 Consolidation–Maintenance protocols for 400 µg of intravitreal MTX. Keeping patience tolerance
15 and toxicity to ocular tissues in mind, therapeutic protocols using 200 µg and 600 µg of intravitreal
16 MTX was developed by analyzing the kinetics of MTX following different doses of intravitreal
17 injection. The release rate of the 90-day controlled release MTX implant should range from 0.5 to
18 2 µg/day in order to maintain therapeutic levels inside the vitreous and retina.

19 **Conclusions:** By making use of the results of this study, one could select a dosing interval for
20 serial injections of MTX or establish a treatment schedule using controlled release implant to treat
21 IOL.

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