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THE INTERACTION OF 6,7-METOXI-VERATRYL-ISOQUINOLEIN(PAPAVERINE) WITH HUMAN HEMOGLOBIN

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Papaverine ($1\text{-}5.10^{-4}$) (PAV) was found to shift the hemoglobin-oxygen dissociation curve of human hemoglobin significantly to the right. The mean P_{50} was increased "in vitro" at physiological buffer (pH7,4) which contained the test compound.

Simultaneously with the shifting of the curve papaverine was found to stabilize the protein T conformation as detected by EPR measurements of the nitrosyl hemoglobin in with the EPR spectrum obtained for the treated hemoglobin shows a displacement towards the spectrum characteristic of T structure, put in evidence by the appearance of the nitrogen structure in the central part of the spectrum.

The stabilization of the T-conformation by PAV in this case is not correlated to the occupation of the polyphosphate by the drug because the cationic nature of PAV. It is possible that the drug can interact directly with the vicinity of the heme-group interfering with the NO binding, as occurs with quinoline.

Equilibrium dialysis was performed to confirm the binding of the drug to the hemoglobin molecule. The time obtained for this equilibrium was 30 hs at the molar ratio Hb/PAV (1/8).

The number of molecules found to bind to hemoglobin was half of the number of Bromotimol Blue that would bind to the hemoprotein.

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