The interaction of some bis-aryl compounds with sites of known structure on human and horse haemoglobin

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The 2,3-diphosphoglycerate (DPG) site on the human haemoglobin molecule has been used as a model pharmacological receptor by Beddell, Goodford, Norrington, Wilkinson & Wootton (1976). However in horse haemoglobin the site has a different structure since residue histamine-β2 is replaced by glutamine (Figure 1). One might therefore expect that the potency of any compound interacting with this residue would be reduced in horse haemoglobin.

Dialdehyde compound I was predicted to react (Figure 1a, b) with the N-terminal amino groups of the β subunits of the protein. Its bisulphite addition complex was also predicted to interact with four histidine residues in human haemoglobin (Figure 1c), but only two in horse haemoglobin (Figure 1d). The observations (Table 1) are compatible with these predictions, and demonstrate how selectivity of drug action may be predicted by the method of receptor fit.

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Reference

BEDELL, C.R., GOODFORD, P.J., NORRINGTON, F.E., WILKINSON, S. & WOOTTON, R. (1976). Compounds designed to fit a site of known structure in human haemoglobin. *Br. J. Pharmac.*, **57**, 201–209.

Table 1 Changes in the oxygen partial pressure at 50% saturation (p50) observed with human and horse haemoglobin by the methods of Beddell *et al.* (1976).

Units	*Conc. (mM)*	*Human p50 (kPa)*	*Horse p50 (kPa)*	*Horse p50 / Human p50*
DPG	2.5	1.78	1.33	0.75
Compound 1	2.5	1.25	1.32	1.06
Compound 1	2.5			
+ Metabisulphite	5	3.15	2.40	0.76
Metabisulphite	5	0.38	0.40	1.05

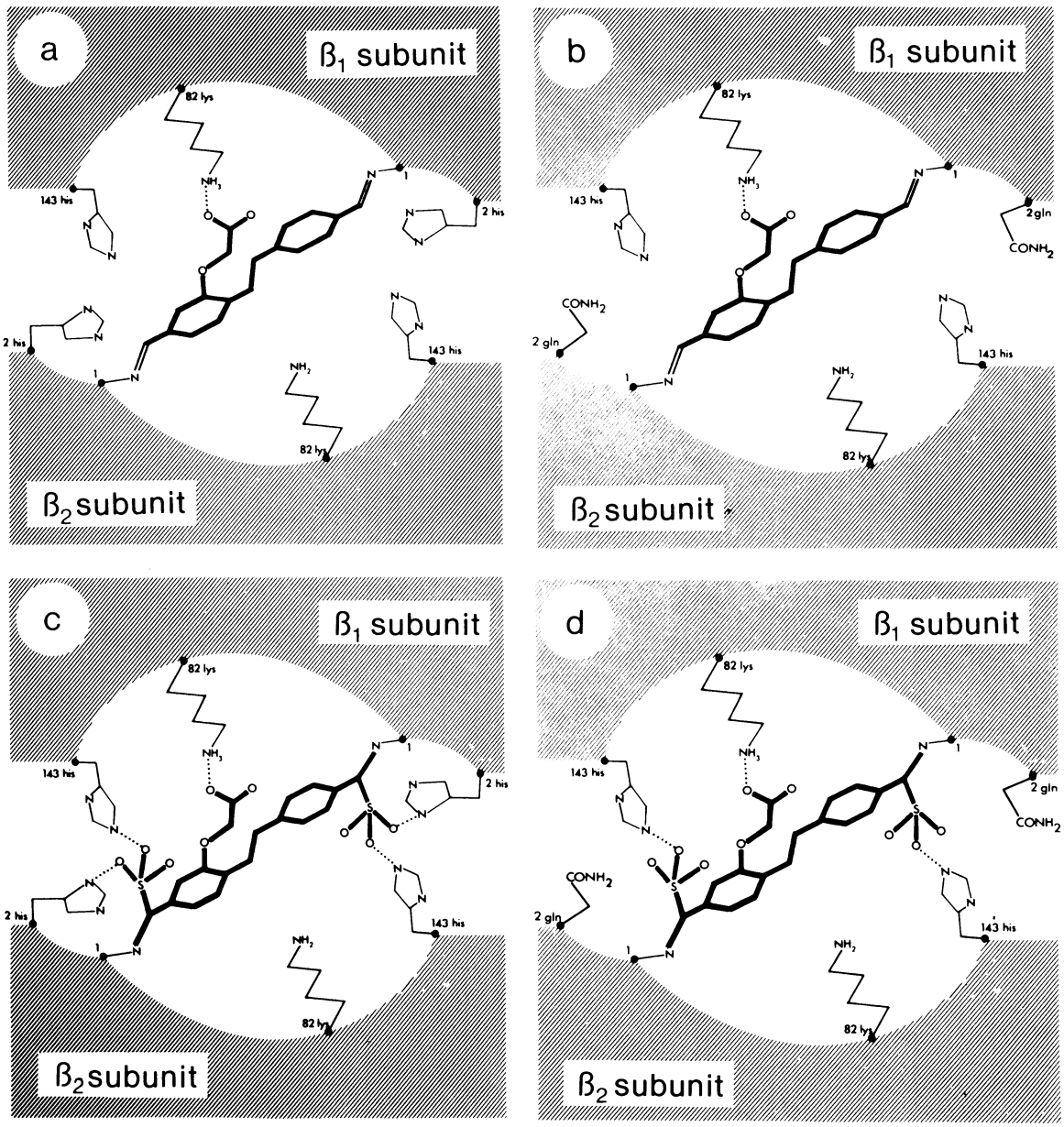

Figure 1 A schematic diagram of the DPG receptor site on (a, c) human and (b, d) horse haemoglobin.