

Analysis of the Composition of a Factor VIII Concentrate, Optivate®.

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INTRODUCTION

Optivate® is a human factor VIII concentrate. The final product also contains von Willebrand Factor (VWF), the natural stabilizer of factor VIII. This study analysed the composition and activity of Optivate® alongside those of a number of other FVIII products.

METHODS

This study assessed the composition of six FVIII concentrate products: Optivate® (BPL), 8Y® (BPL), Fanhdi® (Instituto Grifols, S.A.), Haemate® P (ZLB Behring), Haemoctin® SDH (Biotest Pharma GmbH) and Octanate® (Octapharma Ltd.). Two batches of each product were tested. The products were reconstituted following the manufacturers instructions. The following tests were included in this study: total protein (Pierce™ BCA); FVIII activity (chromogenic); VWF antigen (in-house ELISA), ristocetin co-factor (in-house) and multimer analysis (agarose electrophoresis and western blotting); fibrinogen, fibronectin, FXIII, IgM, albumin (by in-house ELISA); and IgG and IgA (by immunoelectrophoresis).

RESULTS

Table 1— Composition and Activity of Human Factor VIII Concentrates

Product:	8Y	A	B	C	D	Optivate
Protein (mg/mL)	6.3	6.1	8.9	0.5	1.3	2.3
FVIII (IU/mL)	22.7	90.5	48.0	38.0	92.6	95.9
vWF:Ag (IU/mL)	70.9	153	128	18.0	41.2	244
vWF:RCO (IU/mL)	32.1	77.0	99.4	11.1	33.1	133.5
vWFRCO:FVIII (IU/ IU FVIII)	1.4	0.9	2.1	0.3	0.4	1.4
Fibronectin:FVIII (µg / IU FVIII)	31	0.70	0.68	0.27	0.25	0.55
Fibrinogen:FVIII (µg / IU FVIII)	195	0.08	1.3	2.1	2.6	0.74
Factor XIII:FVIII (U/ IU FVIII)	0.02	ND	4.8 x 10 ⁻⁵	ND	ND	2.1 x 10 ⁻⁵
IgA:FVIII (µg / IU FVIII)	1.8	ND	ND/0.2*	ND	ND/0.2*	ND
IgG:FVIII (µg / IU FVIII)	ND	ND	ND	ND	ND	ND
IgM:FVIII (µg / IU FVIII)	2.1	0.12	0.31	0.24	0.19	0.12
Albumin:FVIII (µg / IU FVIII)	1.8	62	174	0.021	0.020	0.018
FVIII Specific Activity (IU/mg protein)	4	15	5	75	71	41
FVIII Specific Activity excluding VWF** protein (IU/mg)	4	19	6	107	98	360

Data are mean value for two batches of each of product as listed in the methods section. ND, none detectable.

* one batch ND.

** assuming 1IU VWF:Ag is equivalent to 8µg

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Figure 1—VWF Multimer Analysis (Low Resolution, Gel 1)

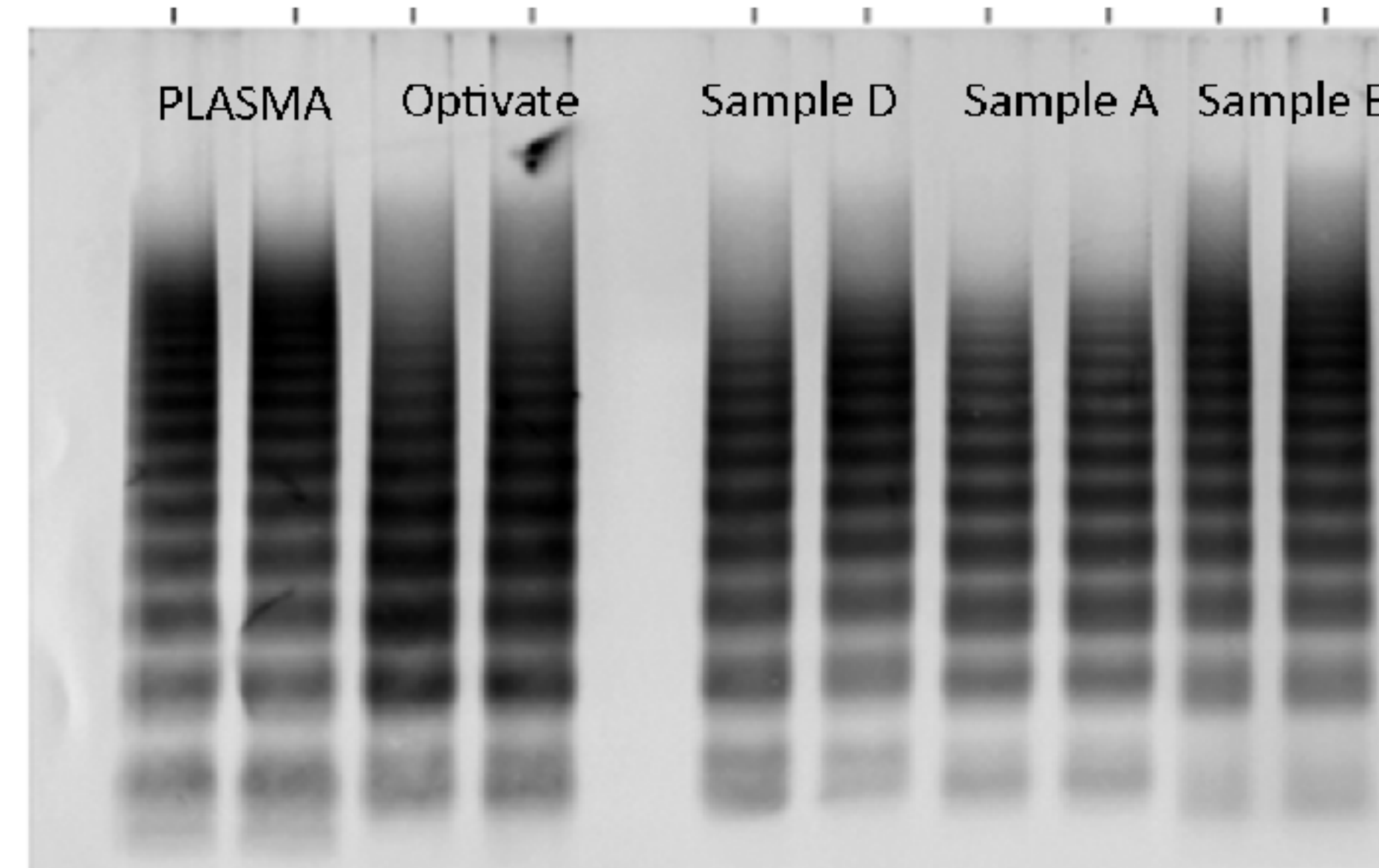


Figure 2—VWF Multimer Analysis (Low Resolution, Gel 2)

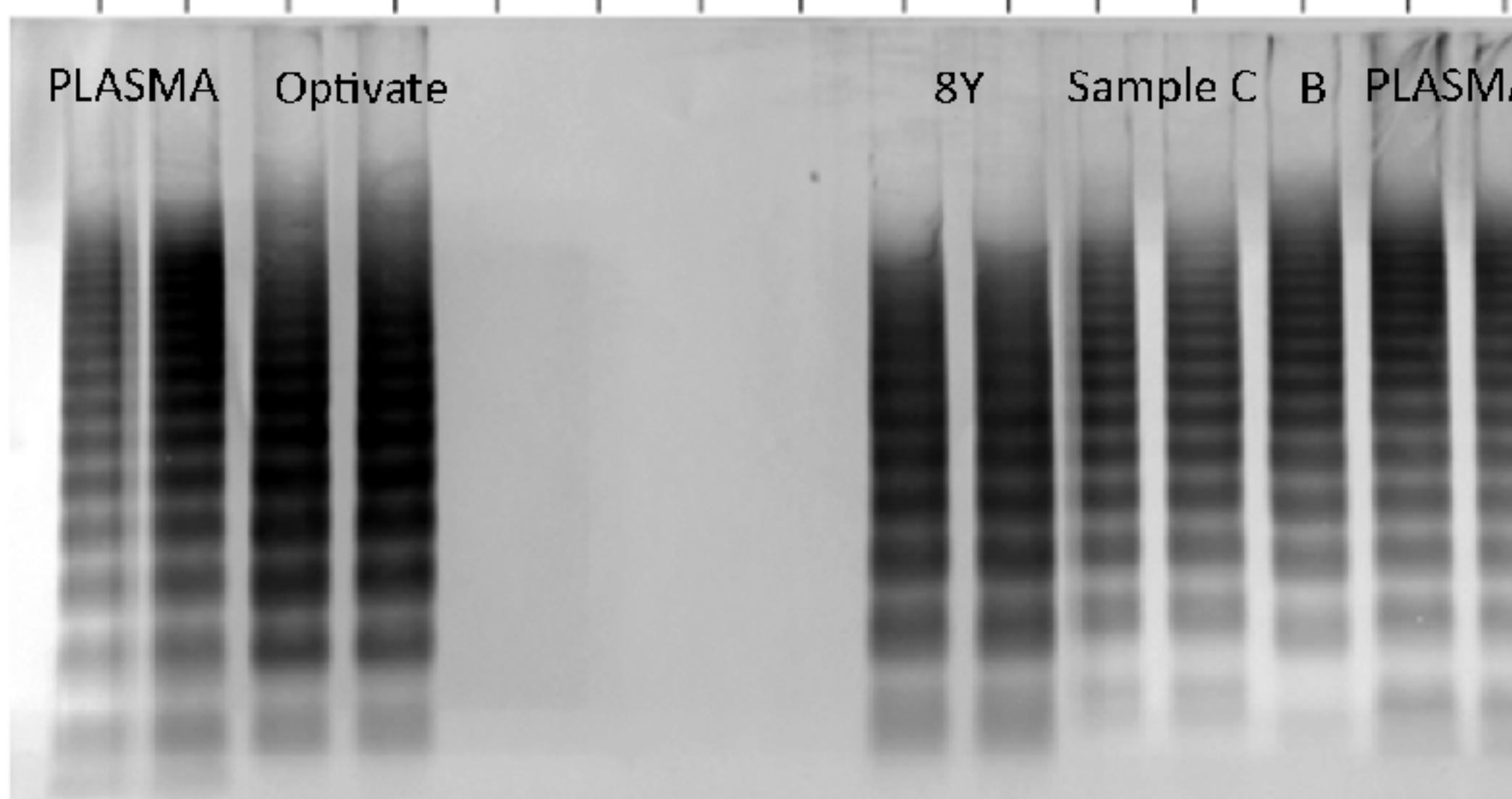


Table 2—Distribution (%) of Low, Medium and High Molecular Weight (MW) VWF Multimers

	% Low MW (Bands 1-5)	Medium MW (Bands 6-10)	High MW (Bands 11+)
Normal Pooled Plasma	30	38	32
8Y®	53	35	11
A	50	36	14
B	39	35	26
C	29	43	27
D	36	42	22
Optivate®	44	35	21

DISCUSSION AND CONCLUSIONS

Optivate® had the highest VWF:Ag concentration of the FVIII concentrates tested here. Likewise Optivate had the highest VWF:RCO potency; its ratio of VWF:RCO to FVIII was the same as 8Y® and only exceeded by one of the other products tested (see Table 1).

All the concentrate batches tested here had similar non-FVIII/VWF protein profiles. However Table 1 shows that Optivate had the lowest level of these non-FVIII/VWF proteins relative to FVIII. This is shown by the individual protein data and highlighted by the FVIII specific activity of Optivate when VWF protein is excluded from the calculation.

All of the FVIII concentrates tested had a similar proportion of medium MW VWF multimer bands as plasma (Table 2 and Figures 1 and 2). The proportion of low and high MW VWF multimers in Optivate was mid-range compared to the other concentrates tested.

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