Optimized Stepwise Synthesis of the API Liraglutide using BAL-resin and pseudo-prolines

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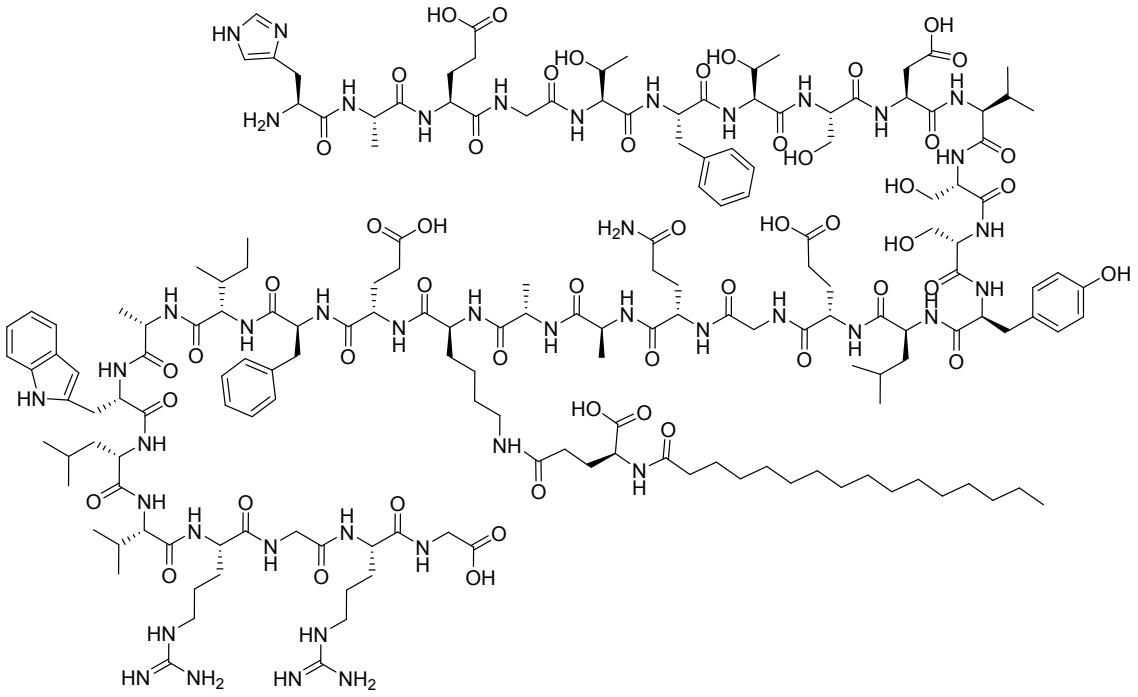

Figure S 1: Sequence of **Liraglutide**

Liraglutide:

Sequence: H - His - Ala - Glu - Gly - ***Thr - Phe - Thr - Ser*** *- Asp -* ***Val - Ser*** - Ser - Tyr - Leu - Glu - Gly - Gln -Ala - Ala - Lys(Palm) - Glu - Phe - Ile - Ala - Trp - Leu - Val - Arg - Gly - Arg - Gly - OH

Use of pseudoprolines was preferred for **bold** amino acids to assure best purities. Amino acids in *Italics* were introduced by using HCTU/DIEA. The rest amino acids were introduced by DIC/OxymaPure cocktail. Crude purity: 84% Yield of synthesis after preparative purification: 69%

Chemical Formula: $C_{172}H_{265}N_{43}O_{51}$ Expected MS of Liraglutide: 3752.3 (M+H). Found MS: 1876.6 $(M+H)^{2+}$, 1251.5 $(M+H)^{3+}$, 938.9 $(M+H)^{4+}$ and 751.2 $(M+H)^{5+}$.

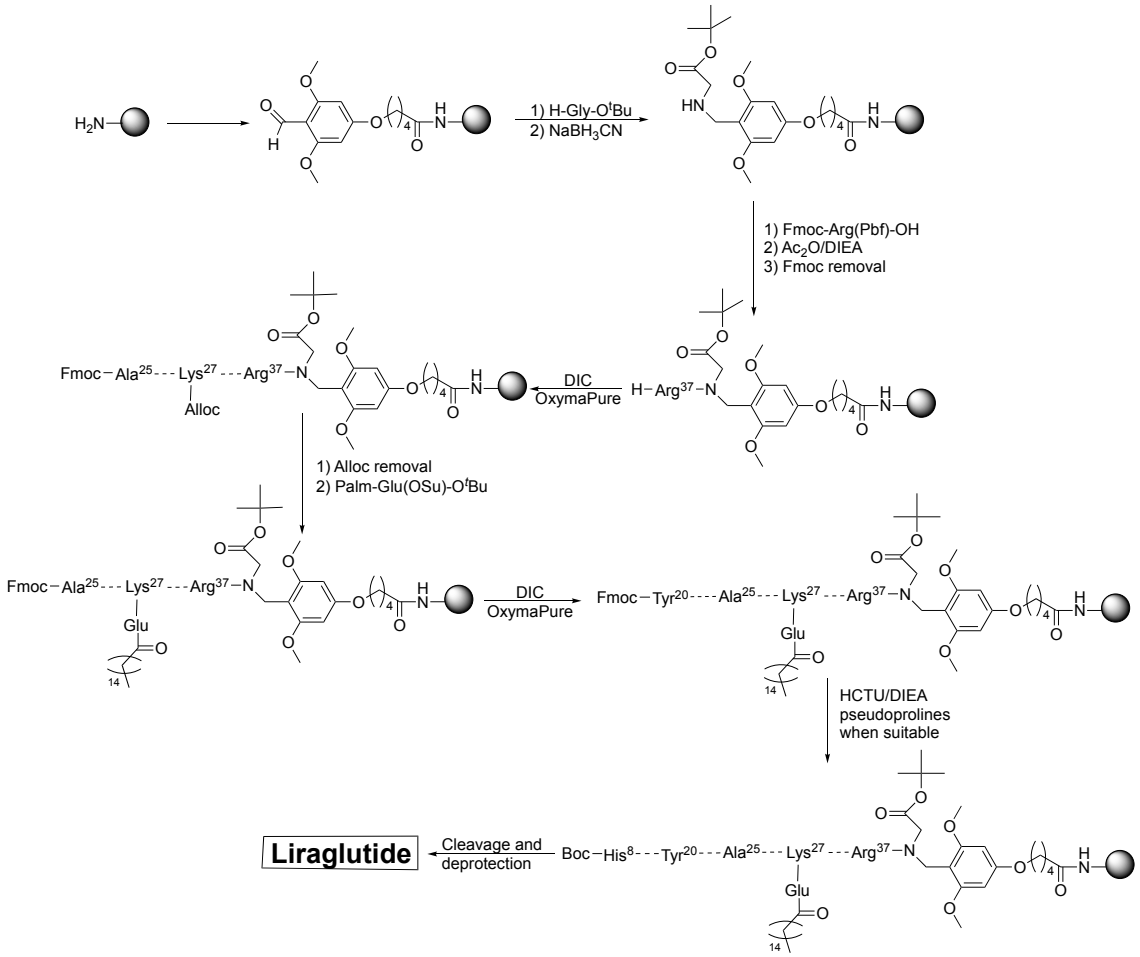

Figure S 2: Detailed final synthetic scheme towards **Liraglutide**

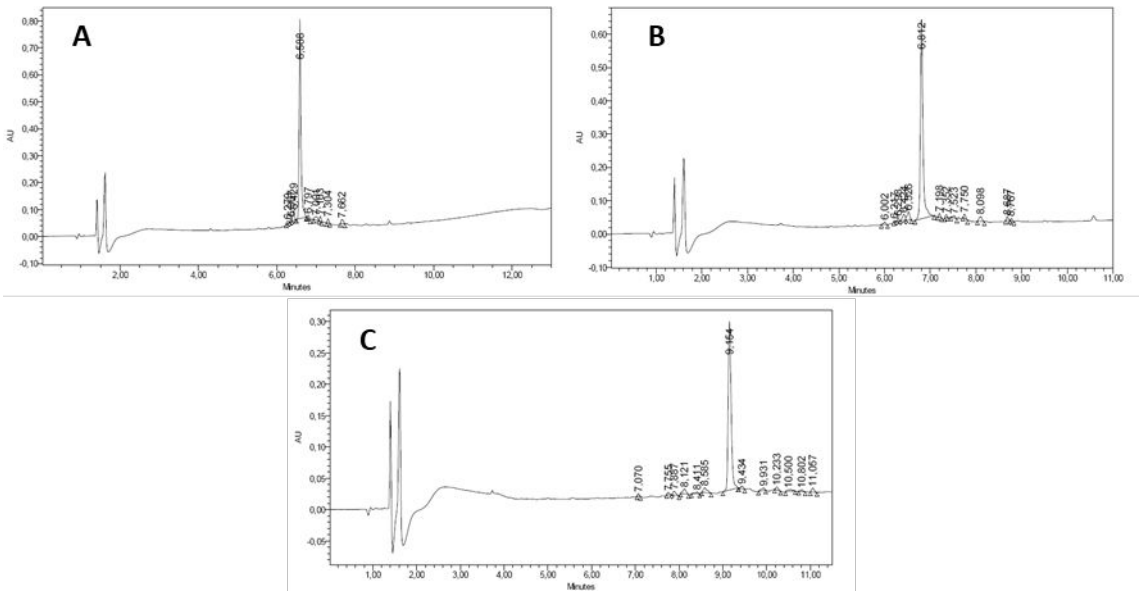

Figure S 3: HPLC traces of crude **Liraglutide.** (**A**) 5-100%ACN (0.1% TFA) in 10min. (**B**) 30-70%ACN (0.1% TFA) in 10min (**C**) 30-50%ACN (0.1% TFA) in 10min. 220nm.

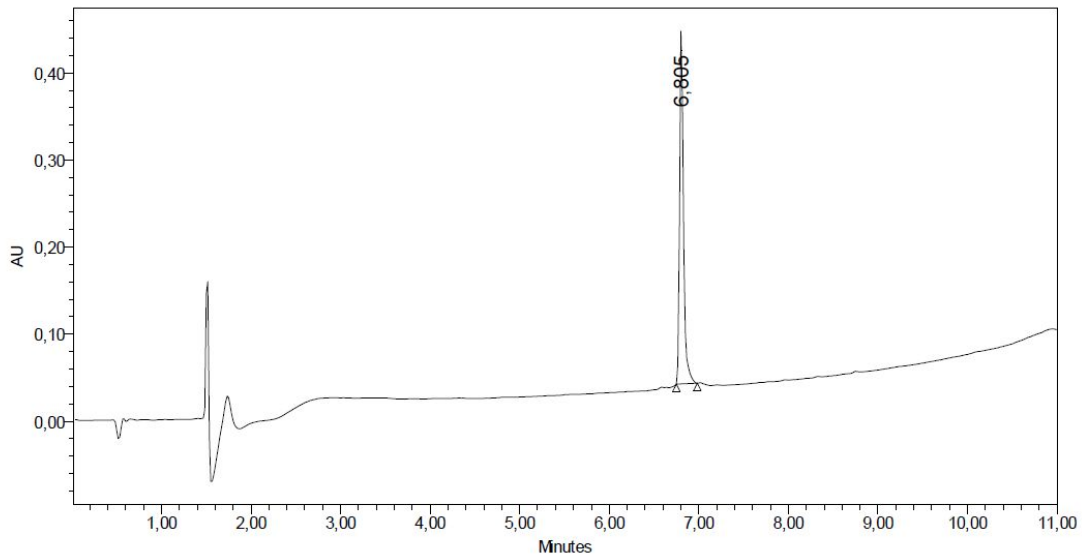

Figure S 4: HPLC trace of pure **Liraglutide.** 5-100%ACN (0.1% TFA) in 10min. 220nm.

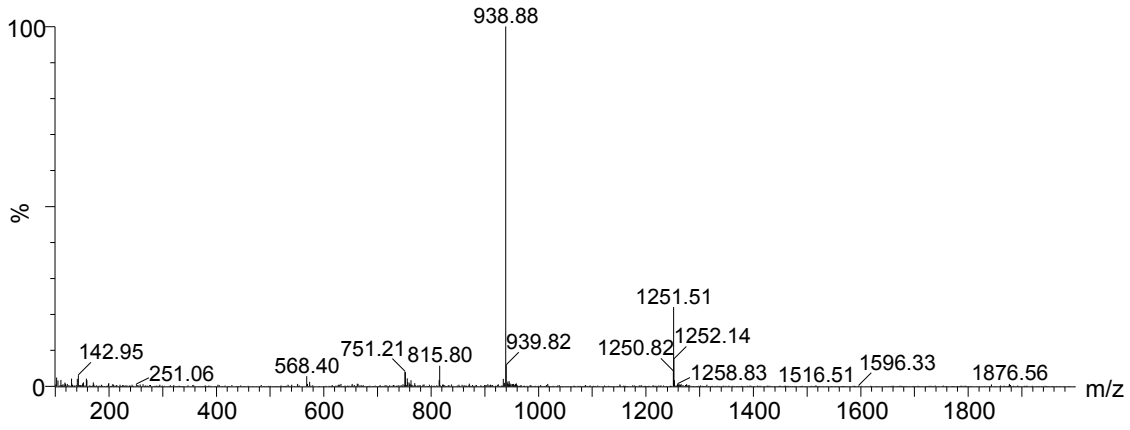

Figure S 5: MS trace of pure **Liraglutide** (ESI)

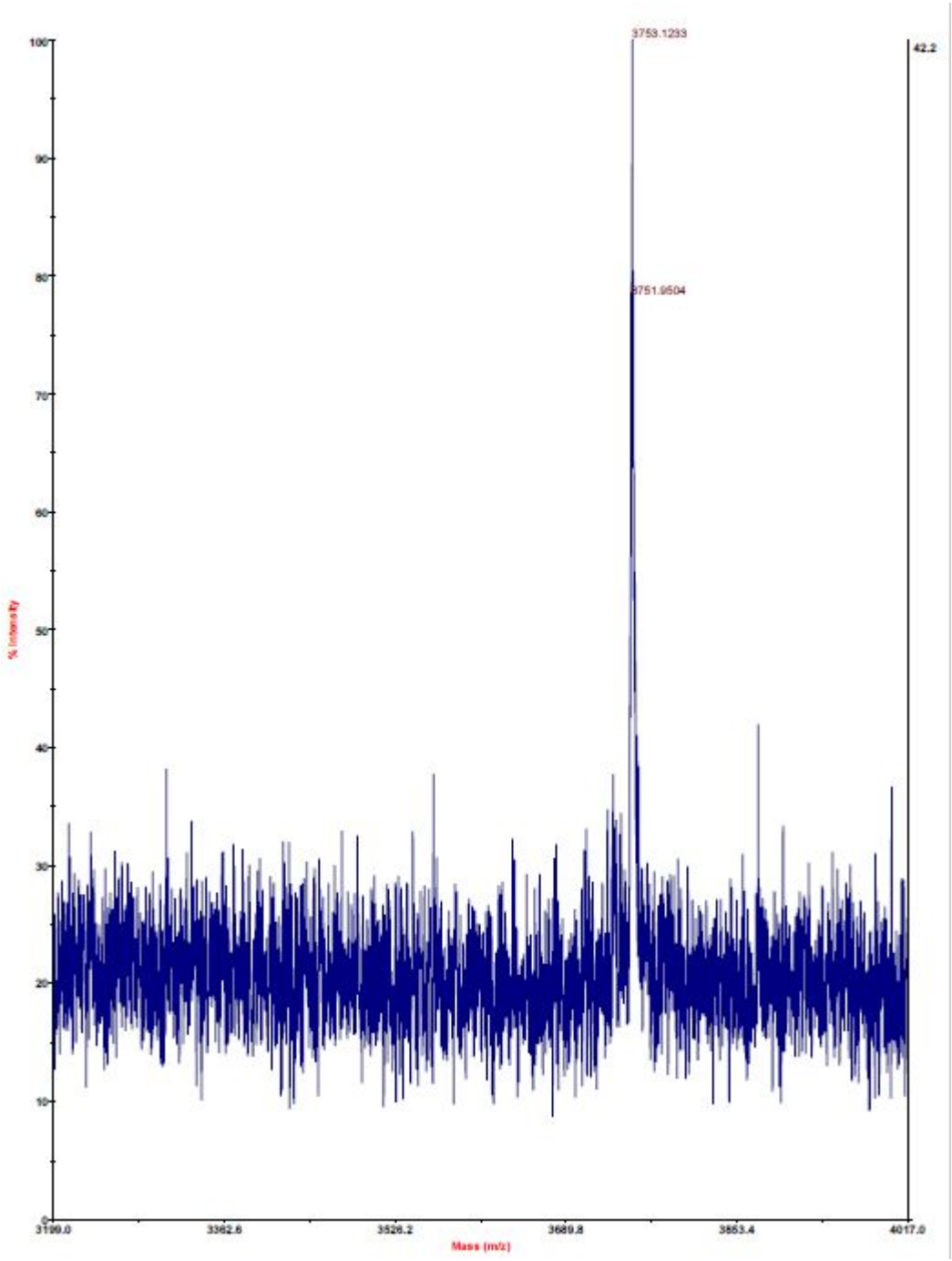

Figure S 6: MS trace of pure **Liraglutide** (MALDI)