INTRODUCTION

Biologically active peptides
Therapeutics, e.g., oncology (buserelin)

1. High temperature exposure • OBJECTIVE
   2. Mechanical shear stress
   3. Polymer/matrix influence

EXPERIMENTAL

Stability indicating UPLC method:
Acquity BEH300 C18 1.7μm (2.1 × 100 mm)
MF A: 95/5 H2O/ACN + formic acid
MF B: 5/95 H2O/ACN + formic acid
1.5 min isocratic hold at 100% A
linear gradient from 0 to 21% B in 9.5 min
7 min isocratic hold

Dry heat conditions

<table>
<thead>
<tr>
<th>T (°C)</th>
<th>150</th>
<th>157.5</th>
<th>165</th>
<th>172.5</th>
<th>180</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time (t) (min)</td>
<td>40</td>
<td>25</td>
<td>15</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>50</td>
<td>30</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>75</td>
<td>45</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>160</td>
<td>100</td>
<td>60</td>
<td>40</td>
<td>40</td>
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</tbody>
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Detection
• DAD-UV (kinetics via normalized areas)
• MS/MS (degradant identification)

Kinetic data evaluation

• Statistical evaluation of 17 solid-state kinetic models [1]:
  ✓ Nucleation (7)
  ✓ Geometrical contraction (2)
  ✓ Diffusion (4)
  ✓ Reaction-order (4)
• Extrapolation to HME-related conditions

RESULTS and DISCUSSION

Kinetic data evaluation per temperature
Ginstling-Brounshtein (Diffusion model): minimal AIC values
1-(2α/3)-(1- α)2T=k×t

Degradiation constant k ∝ temperature T

-10log(K.314xT)

<table>
<thead>
<tr>
<th>Degradation mechanism</th>
<th>pGlu-His-Trp-NH2</th>
<th>pGlu-His-Trp-Tyr-NH2</th>
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</thead>
<tbody>
<tr>
<td>β-elimination + fragmentation</td>
<td>pGlu-His-Trp-Ser-Tyr(ΔBu)-Leu-Arg-Pro-NH-Et</td>
<td>pGlu-His-Trp</td>
</tr>
<tr>
<td>Backbone hydrolysis</td>
<td>Tyr-Ser(ΔBu)-Leu-Arg-Pro-NH-Et</td>
<td>Ala-Tyr-Ser(ΔBu)-Leu-Arg-Pro-NH-Et</td>
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<tr>
<td>Isomerization*</td>
<td>pGlu-His-Trp-Ser-Tyr-Ser(ΔBu)-Leu-Arg-Pro-NH-Et</td>
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Degradant profiling

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<tr>
<th>Degradant profiling</th>
<th>β-elimination</th>
<th>Backbone hydrolysis</th>
<th>Isomerization</th>
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<tr>
<td>(2)</td>
<td>1.</td>
<td>2.</td>
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</table>

CONCLUSIONS

Buserelin (mono acetate) powder in solid state: heat stress analytics by UPLC-DAD/MS

(1) Kinetics: Ginstling-Brounshtein degradation model: HME

REFERENCES

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