STABILITY AND DESOLVATION KINETICS OF DROPÉRIDOL HYDRATES AND AN ETHANOL SOLVATE, STUDIED BY POWDER X-RAY DIFFRACTOMETRY AND DIFFERENTIAL THERMAL ANALYSIS/THERMOGRAVIMETRY

AGRIS BĒRZIŅŠ, ANDRIS ACTIŅŠ, EDGARS SKARBUlis

DEPARTMENT OF CHEMISTRY, UNIVERSITY OF LATVIA
This presentation is provided by the International Centre for Diffraction Data in cooperation with the authors and presenters of the PPXRD symposia for the express purpose of educating the scientific community.

All copyrights for the presentation are retained by the original authors.

The ICDD has received permission from the authors to post this material on our website and make the material available for viewing. Usage is restricted for the purposes of education and scientific research.

PPXRD Website – www.icdd.com/ppxrd      ICDD Website - www.icdd.com
Background

Department of Chemistry, University of Latvia
Droperidol is known to exist in:

- Two polymorphic forms \(^{a,b}\)
- Dihydrate \(^{c}\)
- Hemihydrate \(^{a,b}\)
- Ethanol solvate \(^{d}\)

---


Droperidol hydrates

Dihydrate\textsuperscript{a}

Hemihydrate\textsuperscript{b,c}


Outline

- Droperidol hydrates
  - Sorption-desorption isotherms
  - Dehydration products
  - Dehydration kinetics
  - Lattice parametres of droperidol hemihydrate

- Droperidol ethanol solvate
  - Similarity with hemihydrate
  - Lattice parametres of droperidol ethanol solvate
  - Desolvatation kinetics

- Conclusions
Desorption-sorption isotherms - dihydrate

Desorption-sorption isotherm of droperidol dihydrate in 25 °C temperature
Desorption-sorption isotherms - hemihydrate

\[ \frac{n(H_2O)}{n(droperidol)} \]

Desorption-sorption isotherm of droperidol hemihydrate in 25 °C temperature

Dehydration products - dihydrate

Dehydration of droperidol dihydrate sample A by heating.
Dehydration products - dihydrate

Dehydration of untreated droperidol dihydrate sample C by heating

Int, counts

$\Theta, ^\circ$

$2\Theta, ^\circ$

Intensity, counts

$\Theta, ^\circ$

$2\Theta, ^\circ$

Dehydration of untreated droperidol dihydrate sample C by heating
Dehydration products - hemihydrate

Dehydratation of droperidol hemihydrate by lowering relative humidity (1)
Dehydration products - hemihydrate

Dehydration of droperidol hemihydrate by lowering relative humidity (2)
Droperidol hydrates - conclusions

- **Droperido dihydrate**
  - typical stoichiometric hydrate
  - complicated dehydration process

- **Droperidol hemihydrate**
  - typical nonstoichiometric hydrate
  - Dehydration gives isomorphous dehydrate
Dehydration kinetics – dihydrate

Dehydration kinetic curves of droperidol dihydrate sample A in nitrogen flow with sample mass 5 mg
Dehydration kinetics – dihydrate (3)

After optimization obtained least square sums for most appropriate kinetic models for droperidol dihydrate sample A with sample mass 5 mg
With optimization method calculated activation energy values for droperidol dihydrate samples
Dehydration kinetics – hemihydrate (1)

Dehydration kinetic curves of grinded and ungrinded droperidol nonstoichiometric hydrate
Dehydration kinetics – hemihydrate (1)

With optimization method calculated activation energy values for droperidol nonstoichiometric hydrate samples.
Hemihydrate water content influence on lattice parameters

![Graph showing the influence of hemihydrate water content on lattice parameters.](image)

Hemihydrate water content influence on lattice parameters (2)
Hemihydrate water content influence on lattice parameters (3)
Hemihydrate water content influence on lattice parameters (4)
Droperidol ethanol solvate

PXRD patterns of droperidol nonstoichiometric hydrate and ethanol solvate
Droperidol ethanol solvate structure

Structure of droperidol ethanol solvate

Sorption-desorption isotherm of droperidol ethanol solvate

\[ \frac{n(\text{EtOH})}{n(\text{droperidol})} \]

- **Global model**
- **Disordered ethanol**
- **Langmuir model**

\[ X(\text{EtOH}), \% \]

---

Lattice parameter changes

![Graph showing lattice parameter changes as a function of n(EtOH)/n(drop).]
Lattice parameter changes (2)
Desolvatation kinetics

Desolvation kinetic curves of droperidol ethanol solvate
Desolvatation kinetics (2)

\[ \alpha = 1 - (Ae^{-ka t} + Be^{-kb t}) \]

\[ R^2 = 0.9994 \]

- Biphasic model
  - Component A
  - Component B

Component A and B weight in kinetic curves of droperidol ethanol solvate


<table>
<thead>
<tr>
<th>Biphasic model, component A</th>
<th>( E_a = (55 \pm 4) \text{ kJ} \cdot \text{mol}^{-1} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biphasic model, component B</td>
<td>( E_a = (67 \pm 5) \text{ kJ} \cdot \text{mol}^{-1} )</td>
</tr>
</tbody>
</table>
Conclusions

- Droperidol dihydrate is stoichiometric and its hemihydrate actually is nonstoichiometric hydrate.
- Dehydration-hydration of nonstoichiometric hydrate is reversible while that of dihydrate is irreversible.
- Dehydration of dihydrate can be described with Avrami-Erofeev while dehydration of nonstoichiometric hydrate can be described with first order kinetic model.
Conclusions (2)

- Nonstoichiometric hydrate’s and ethanol solvate’s lattice parameters systematically changes depending on solvent content in the structure.

- Most effective hydrogen bond structure in nonstoichiometric hydrate is for hemihydrate stoichiometry.

- Almost maximum ethanol content in ethanol solvate are reached when ethanol content in atmosphere is about 5%.

- Ethanol solvate desolvatation can be described with biphasic model.
Thank you for your attention!

Acknowledgments:
• Riga Technical University Institute of Inorganic Chemistry
• Liāna Orola
• European Social Fund for a scholarship to A. Bērziņš and Latvian Academy of Sciences Grant.
• JSC Grindeks for droperidol samples