Stability studies of commercial corticosteroid suspensions

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Introduction

- Steroids are drugs used as anti-inflammatory agents for several indications
  - Particulate corticosteroids : suspension of corticosteroids. The active ingredient dissolves slowly and their therapeutic effect last longer (weeks to months)
  - Non-particulate corticosteroids : solution of corticosteroids. The molecules are eliminated more rapidly and their therapeutic effect last only a few days or weeks

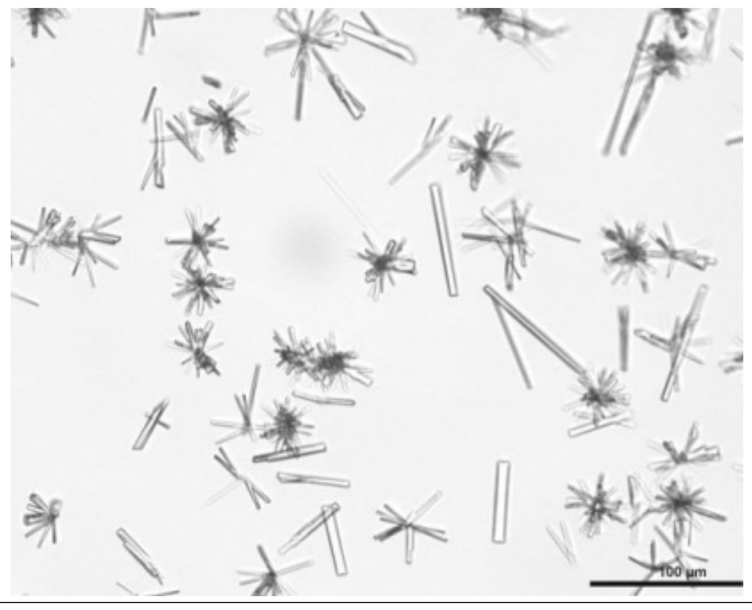
- Injectable corticosteroids are used to treat back pain

- Particulate steroids used in epidural injections have been suspected to be the cause of serious post-procedural embolic events
  - Neurovascular embolization
  - Spinal cord injury
  - Paralysis
  - Death

- These events are caused by microparticles entering the circulation when blood vessels are injured during the procedure, thereby blocking the capillary

Aim of the study: Measure the particle size of commercial corticosteroid suspensions and their stability under conditions that simulate the biological environment
- acidic pH, co-incubation with local anesthetics and contrast agents, presence of albumin

Figure 1. Microscopic image of particles [2]



References

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[2] Watkins TW, Dupre S, Coucher JR. Ropivacaine and dexamethasone: a potentially dangerous combination for therapeutic pain injections. J Med Imaging Radiat Oncol. 2015;59(5):571-577.

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Results and Discussion

Particle size of corticosteroid suspensions

- The particles were measured in saline
- The median particle size of individual corticosteroids ranges from [5.8 - 21.4] µm
- All corticosteroid suspensions contain particles larger than erythrocytes which have a diameter between [6.2 – 8.2] µm

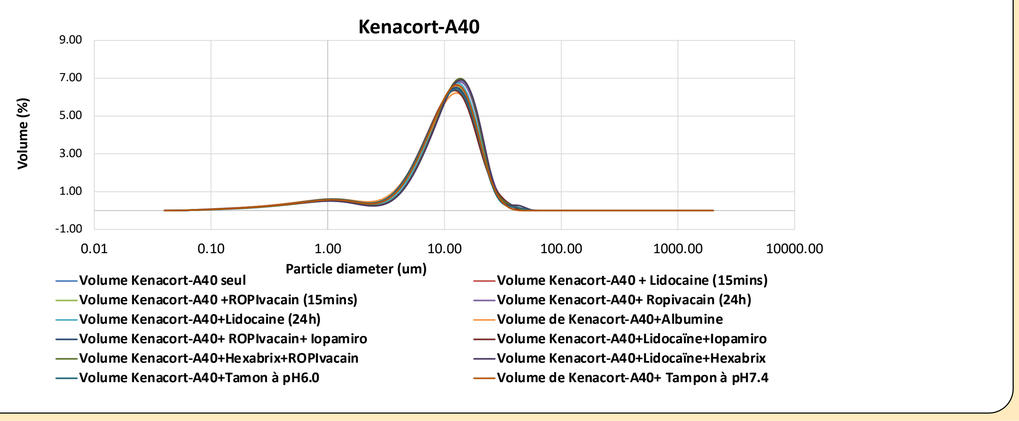
Figure 2. Size of individual particle of corticosteroids

Corticostéroides	D10 en (µm)	D50 en (µm)	D90 en (µm)
Kenacort-A10mg/mL	2.0 ±0.1	11.5 ±0.4	22.6 ±0.4
Kenacort-A40 mg/mL	2.2 ±0.4	11.7 ±0.8	21.4 ±0.8
Triamcort-Depot 10mg/mL	1.6 ±0.1	10.5 ±0.1	18.9 ±0.1
Triamcort-Depot 20mg/mL	1.4 ±0.1	9.4 ±0.9	17.0 ±1.1
Triamcort-Depot 40mg/mL	1.4 ±0	10.6 ±0.4	18.6 ±0.5
Triamcort-Depot 80mg/2mL	1.5 ±0.1	9.7 ±0.6	17.2 ±0.7
Triamject 20mg/mL	1.8 ±0.0	5.8 +0.0	11.8 ±0.1
DEPO-Medrol 40mg/mL	2.0 ±0.1	10.7 ±0.6	17.8 ±0.8
DEPO-Medol 80mg/mL	2.2 ±0.5	12.5 ±0.2	20.7 ±0.6
DEPO-Medrol 200mg/5mL	2.0 ±0.5	11.1 ±0.3	18.7 ±0.1
Diprophos 2mg + 5mg/mL (Ampoule)	4.3 ±0.3	15.3 ±0.4	26.2 ±0.6
Diprophos 2mg + 5mg/mL (injection)	6.9 ±0.7	21.4 ±1.0	35.5 ±1.5

Particle size in different biomimetic media

- Particle size measurements are
  - Mixed with a buffer at pH = 7.4 and a buffer at pH = 6
  - Mixed with an anesthetic agent
  - In presence of a plasma protein (albumin)
  - Mixed with anesthetic agents and contrast agents
- These conditions did not change the size of the particles. There is only one exception ; DEPO-Medrol in the presence of albumin.

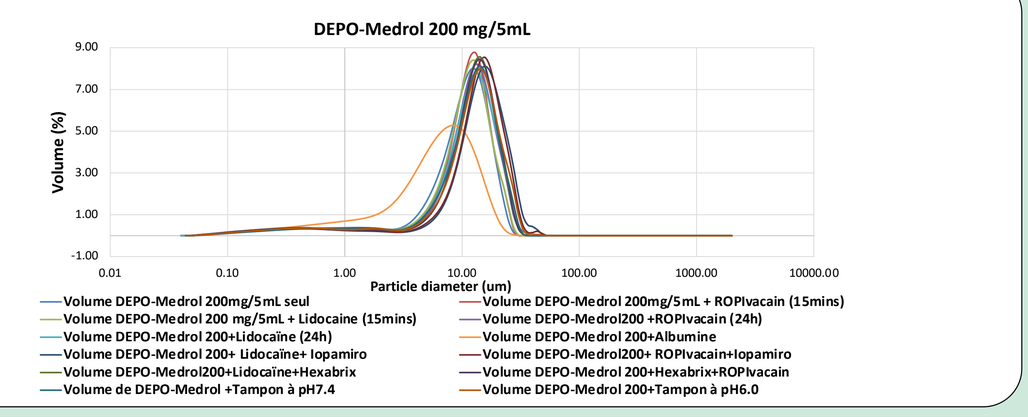
Figure 3. Example of a result of a drug at different conditions



Change in particle size of DEPO-Medrol

- A decrease was observed in the particle size of DEPO-Medrol 200mg/5mL ; from 11.1 µm to 6.2 µm when mixed with albumin.
- Hypothesis : the change in size in the presence of albumin is due to the increased dissolution of DEPO-Medrol

Figure 4. DEPO-Medrol profil at different conditions



Conclusions

- Epidural administration of corticosteroid suspension has been associated with thromboembolic events.
- Particle size of commercial corticosteroid suspensions were larger than erythrocytes in all formulations in this study ; all suspensions have the ability to block vessels.
- Most of the conditions (biological environment) did not change the size of the particles. The only exception was DEPO-Medrol in the presence of albumin.