Comparative and Optimization of administration of Dexlansorazole through nasogastric tubes using an oral liquid vehicle as a suspending agent

1.0 INTRODUCTION
Proton pump inhibitors (PPIs) are widely used for the treatment of various acid-related disorders. For intensive care patients Stress-induced gastrointestinal tract bleeding (SGIB) is common, Dexlansoprazole is a PPI that suppresses gastric acid secretion by specific inhibition of the (H⁺,K⁺)-ATPase in the gastric parietal cell. The aim of this study was to compare the behavior of the dexlansoprazole during the transit of the pellets through the nasogastric tube and to optimize the mode of administration. In this experiment we designed to study the influence of four variables: the tube material (silicone or polyurethane), the solvent used to disperse the pellets (water or apple juice), the mode of administration and the rinse volume. We counted the pellets before administration to tube and at the tube outlet, and assayed the dexlansoprazole by UV spectrometry. The assay showed that transit of dexlansoprazole through the tube was nearly 85.5 to 99.6%. There is significant improvement was obtained by the variables ‘diluent’ and ‘mode of administration’. The variable ‘rinse’ had a significant influence. Dexlansoprazole is thus the choice of Proton pump inhibitor for the treatment of patients by nasogastric tube, using a polyurethane tube and a rinse 10 ml of apple juice.

Keywords: Dexlansoprazole, water, apple juice and nasogastric tube.

2.0 MATERIALS AND METHODS
2.1 Materials:
Dexlansoprazole DR capsules 30 mg (Kapedex) was supplied by Tap pharmaceuticals and formulated in our lab. The dexlansoprazole DR capsules was formulated in gelatin capsules containing enteric coated pellets or pellets which are gastric resistant pellets. The pellets were dispersed in apple juice or water, and injected into the nasogastric tube using a 60 ml catheter-tip syringe with the plunger (Becton Dickinson). Two types of 16 French gauge gastroduodenal tubes were used: polyurethane tubes.
(Salem type, length 120 cm, internal diameter 3.8 mm) and silicone tubes (Levin type, length 125 cm, internal diameter 3 mm, Vygon). Apple juice (Tropicana 100%, 1284CB, Schreiber Dynamix Dairies) and purified water.

2.2 Method:
The administration solvents (Water and apple juice) and NG tubes used in our experiments were chosen as closely as possible to those commonly used in intensive care to compare the recovery of kapidex and our lab product.

Administered the dexlansoprazole pellets through the nasogastric tube positioned (figure 1), as it would be in a reclining patient. In this study we observed the influence of four variables: the 16 French gauge tube material (silicone or polyurethane), the nature of the solvent (water or apple juice), the rinse volume and the administration pattern. We have carried out 16 separate experiments (Table 1), each repeated three times. Before each administration, the tubes were rinsed with the solvent chosen to carry the pellets.

Procedure:
One Dexlansoprazole 30-mg capsule was then opened and the pellets emptied into 60 ml catheter-tip syringe. Added water or apple juice to the syringe up to the mark. The plunger was then replaced and, with the tip up, the syringe side to side shaken until the pellets in the tip moved into the body of the syringe. The syringe containing the mixture was always shaken during the administration to prevent pellets adhering to the syringe wall and the tip requires elevation and lowering to prevent accumulation of the pellets near the tip and we maintained a constant flow rate of injection to limit tube obstruction. The pellets were then recovered in a plastic beaker placed under the end of the tube and repeat the same for Kapidex as mentioned in table 1.

2.3. Analysis of samples:
The pellets were collected at exit of tube, counted and were analyzed for assay of dexlansoprazole to compare the Kapidex to our lab product.

2.3.1. Assay of active ingredient
The suspension of pellets collected at the tube exit was filtered on a 0.45 mm screen to recover the pellets. These were then dissolved in pure methanol. After complete dissolution by sonication, the suspension filtered through 0.45 micron filter. The clear solutions obtained were then diluted 10-fold and assayed by UV spectrophotometry at 285 nm. We determined the percentage of active ingredient recovered at the tube exit relative to the initial dose injected into the tube.

2.3.2. Counting of pellets
In addition to the assay, the pellets were counted before and after transit through the tube.

Figure 1: Tubing position
Table 1: Experiments performed to compare the impact of material-related and administration pattern-related parameters on dexlansoprazole transit through nasogastric tubes

<table>
<thead>
<tr>
<th>No. of trails</th>
<th>Material of tubing</th>
<th>Solvent</th>
<th>No. of pellets</th>
<th>Administration volume (mL)</th>
<th>Rinse volume (mL)</th>
<th>Recovery of pellets</th>
<th>Recovery of assay (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Silicone</td>
<td>Water</td>
<td>275</td>
<td>1x40</td>
<td>NA</td>
<td>235</td>
<td>85.7</td>
</tr>
<tr>
<td>2</td>
<td>Silicone</td>
<td>Apple juice</td>
<td>269</td>
<td>1x40</td>
<td>NA</td>
<td>252</td>
<td>93.8</td>
</tr>
<tr>
<td>3</td>
<td>Silicone</td>
<td>Water</td>
<td>277</td>
<td>1x30</td>
<td>10</td>
<td>257</td>
<td>92.2</td>
</tr>
<tr>
<td>4</td>
<td>Silicone</td>
<td>Apple juice</td>
<td>271</td>
<td>1x30</td>
<td>10</td>
<td>268</td>
<td>95.6</td>
</tr>
<tr>
<td>5</td>
<td>Polyurethane</td>
<td>Water</td>
<td>279</td>
<td>1x40</td>
<td>NA</td>
<td>251</td>
<td>89.7</td>
</tr>
<tr>
<td>6</td>
<td>Polyurethane</td>
<td>Apple juice</td>
<td>270</td>
<td>1x40</td>
<td>NA</td>
<td>264</td>
<td>97.8</td>
</tr>
<tr>
<td>7</td>
<td>Polyurethane</td>
<td>Water</td>
<td>267</td>
<td>1x30</td>
<td>10</td>
<td>253</td>
<td>94.6</td>
</tr>
<tr>
<td>8</td>
<td>Polyurethane</td>
<td>Apple juice</td>
<td>274</td>
<td>1x30</td>
<td>10</td>
<td>272</td>
<td>99.2</td>
</tr>
</tbody>
</table>

* For each experiment, three assays were done.

3.0 RESULTS

The assay of the dexlansoprazole showed a recovery rate of 85.7 to 99.6% with significant variations between administration pattern and solvent. No significant difference was found regarding concentration of active ingredient or quantity of pellets obtained at the tube exit.

In this study, we observed a significant change in the quantity of pellets collected from one administration pattern to another (85.2 to 99.6% of dexlansoprazole recovered, with a variability of about 15%). The ‘solvent’ and ‘administration pattern’ factors gave significant improvement in the recovery of pellets. The ‘rinse volume’ also influenced the recovery of pellets.

4. DISCUSSION

4.1.1. Influence of administration pattern

We investigated whether it was preferable to administer the dexlansoprazole pellets. Hence, the administration pattern also influenced the recovery of pellets by using different administration patterns, rinse volume.

4.1.2. Influence of solvent

In intensive care patients the solvents most often used are water and fruit juice (e.g., apple juice, orange juice). We consider apple juice (pH:3.2) because it maintains an acidic medium. The enteric coating pellets maintain and shows gastro-resistance property when they arrive in the stomach. Accordingly, we preferred to focus our study on the two solvents recognised as being suited to the administration of dexlansoprazole by nasogastric tube: water and apple juice. When we used water and apple juice the recovery was observed 72% and 86%. Finally the study shows that there is a significant difference to recovery of pellets between these two solvents to recover the pellets.

4.1.3. Influence of dosage form
The analysis of pellet size suggested some possible explanations for the tube obstruction observed and demonstrated by measurement of the pellets and by the inconsistency of the pellet size based on concentrations and quantities of pellets obtained. All the administrations of dexlansoprazole was accompanied by a dual evaluation of the final quantity recovered: by assay and by counting of pellets. This dual evaluation revealed the variations in pellet size.

4.2.2. Influence of nature of tubing

We observed that the nature and material of the tube played a significant role in the delivery of dexlansoprazole DR pellets (polyurethane tubes favoured the flow of dexlansoprazole pellets). However, it is impossible to correlate this difference to the tube material because for the same gauge (16 French), the two types of tube used did not have the same internal diameter. The 16 French gauge silicone tube had a smaller internal diameter than the 16 French polyurethane tube (3mm versus 3.8 mm). Thus, the influence of the tube material on the behaviour of the dexlansoprazole pellets is not precisely known.

5.0 CONCLUSION

Based on the above data, 99.0 % of pellets recovered from polyurethane nasogastric tube (16F) with apple juice as a solvent for both Kapidex and our lab products are similar in nature. Hence dexlansoprazole is the choice for the treatment of intensive care patients through a nasogastric tube using a polyurethane tube, apple juice 30 ml as a solvent and 10 ml as a rinse for the administration can be considered.

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7.0 REFERENCES


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