Spectrophotometric determination of acetaminophen content of different brands of paracetamol tablets from Zliten

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INTRODUCTION:

Paracetamol is a medicine compound commonly used as analgesic and antipyretic.\(^1\)\(^-\)\(^5\) It is classified as one of the drugs, known as aniline analgesics.\(^6\)\(^-\)\(^9\) It is used widely for the relief of a headache, other minor aches, pains, inflammations and a major ingredient in several cold and flu remedial combination drugs. While generally safe for use at a recommended dose, toxicity of paracetamol is the foremost cause of acute gastrointestinal problems.\(^10\)\(^-\)\(^12\) Paracetamol is considered to be the inhibitor of cyclooxygenase (COX), and recent reports suggest that it is highly selective for COX-2. While it has analgesic and antipyretic properties comparable to those of aspirin or other NSAIDs, its peripheral anti-inflammatory activity is usually limited by several factors, one of which is high level of peroxides present in inflammatory lesions. It could be considered as one of Non-Steroidal Anti Inflammatory Drugs (NSAID).\(^13\)\(^-\)\(^20\) Many methods for its determination have been described in literature, including chromatography (RP - HPLC), chemometric - assisted spectrophotometric spectroscopy, Spectrophotometry and electrochemistry.

Many spectrophotometric methods required complicated treatment, such as long period of heating (60-90 min) using concentrated acids as hydrolysis reagent. This work based on the oxidation of paracetamol by using Cr(VI) in presence of 6M sulfuric acid and 15 min heating at 80 °C as shown in scheme 1.

Results:

In this method, paracetamol is deacetylated to \(p\)-aminophenol in the first step, then oxidised by potassium dichromate to benzoquinone (scheme 1), and the absorbance of
the chromium (IV) species produced at 580 nm, is the measure of paracetamol concentration. Paracetamol was prepared in the laboratory by a method described by vogel. The material was checked by melting point and found within the recorded rang (168-172 °C) and used as a stock material. Then 13 different medicines contain paracetamol as the main ingredient were collected from different pharmacies around the city of Zliten, and taken under the study to measure paracetamol concentration in them.

Scheme 1 shows the steps of paracetamol oxidation.

Table 1 shows the concentrations of paracetamol in the 13 medicines which supplied by different companies compared with the pure paracetamol. From that table, it can be seen that some of medicine have paracetamol within the right concentration (2-5). While some drugs contain higher concentration than what it is included in their leaflet (13, 14) and some have lower than the provided amounts.

**Discussions:**
The excess or the lack of acetaminophen contents obtained in the spectrophotometric results using by this method may be due to the effect of interference i.e. the excipients used in formulation. Any ingredients added to paracetamol formulation contain aromatic amine, it is likely to interfere with the determination of active in the paracetamol tablet. The commonly used preservatives in the formulation of paracetamol in most of the pharmaceutical companies in Nigeria are methyl and propyl paraben. Other additives may include Talcum powder to give shining and smoothness to the tablet, starch as binding agent, magnesium stearate as lubricant, gelatine and lactose.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Form</th>
<th>Commercial name</th>
<th>Supplier</th>
<th>Paracetamol found (mg)</th>
<th>Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Paracetamol (100 mg)</td>
<td>Powder</td>
<td>-</td>
<td>Lab made</td>
<td>100</td>
<td>-</td>
</tr>
<tr>
<td>2 Paracetamol (500 mg)</td>
<td>Tablet</td>
<td>Paracetamol</td>
<td>England</td>
<td>100.6</td>
<td>+0.6</td>
</tr>
<tr>
<td>3 Paracetamol (500 mg) + caffeine 65 mg</td>
<td>Tablet</td>
<td>Paracetamol with caffeine</td>
<td>England</td>
<td>495</td>
<td>-5</td>
</tr>
<tr>
<td>4 Paracetamol (500 mg)</td>
<td>Effervescent tablet</td>
<td>Paracetamol IPS</td>
<td>Tunisia</td>
<td>490</td>
<td>-10</td>
</tr>
<tr>
<td>5 Paracetamol (500 mg)</td>
<td>Effervescent tablet</td>
<td>Doliprane</td>
<td>Germany</td>
<td>483</td>
<td>-17</td>
</tr>
<tr>
<td>6 Paracetamol (500 mg)</td>
<td>Effervescent tablet</td>
<td>Doliprane</td>
<td>Tunisia</td>
<td>477</td>
<td>-23</td>
</tr>
<tr>
<td>7 Paracetamol (400 mg) + Ascorbic acid (300 mg) + Ibuprofen (200 mg) + Caffeine (25 mg)</td>
<td>Powder</td>
<td>Rhumix</td>
<td>Marroco</td>
<td>375</td>
<td>-25</td>
</tr>
<tr>
<td>8 Paracetamol (325 mg)</td>
<td>tablet</td>
<td>Really Extra</td>
<td>India</td>
<td>254</td>
<td>-46</td>
</tr>
<tr>
<td>9 Paracetamol (325 mg), Ibuprofen (200 mg)</td>
<td>Tablet</td>
<td>Megafen</td>
<td>Egypt</td>
<td>224</td>
<td>-101</td>
</tr>
<tr>
<td>10 Paracetamol (500 mg)</td>
<td>Tablet</td>
<td>Cetamol</td>
<td>Tunisia</td>
<td>312</td>
<td>-188</td>
</tr>
<tr>
<td>11 Paracetamol (500 mg)</td>
<td>Tablet</td>
<td>Panadol</td>
<td>Tunisia</td>
<td>300</td>
<td>-200</td>
</tr>
<tr>
<td>12 Orphendrine Citrate 35 mg</td>
<td>Tablet</td>
<td>Muscadol</td>
<td>UEA</td>
<td>197</td>
<td>-303</td>
</tr>
<tr>
<td>No</td>
<td>Description</td>
<td>Form</td>
<td>Brand</td>
<td>Country</td>
<td>Price Difference</td>
</tr>
<tr>
<td>----</td>
<td>------------------------------------------</td>
<td>---------------</td>
<td>------------</td>
<td>---------</td>
<td>------------------</td>
</tr>
<tr>
<td>13</td>
<td>Paracetamol 450 mg + Orphendrine Citrate 35 mg</td>
<td>Tablet</td>
<td>Norgesic</td>
<td>Egypt</td>
<td>645 +195</td>
</tr>
<tr>
<td>14</td>
<td>Paracetamol (500 mg)</td>
<td>Tablet</td>
<td>Adol</td>
<td>UEA</td>
<td>763.5 +263.5</td>
</tr>
</tbody>
</table>
Conclusion:
This work shows that the low or high values of paracetamol concentrations in pharmaceuticals compared to the expected values could be due to poor drug control, as well as the state of chaos in the country and its consequent smuggling and misstorage, which leads to rapid spread among patients due to cheap prices and thus do not have effective effect.

Experimental:

Apparatus:
A JENWAY- SPEC/6400, 520 ×330 × 180 mm :Rs 232 output, band width of 5 nm Scanning Visible Spectrophotometer with recording unit and matched a set of 1 cm. glass or quartz cuvettes were used for recording the spectra. All the weighing measurements were made by a Shimadzu-AUX-220 model digital electronic balance.

Reagents:
Stock solutions were made from commercially available analytical or pharmaceutical grade chemicals and high purity distilled water. Working solutions were prepared by appropriate dilution of the stock solutions. The 0.135M potassium dichromate solution was prepared in 12M sulphuric acid.
Paracetamol solutions (1 mg/ml) were also prepared from pharmaceutical-grade tablets and capsules. The pure stock solution was prepared by dissolving exactly 0.500 g in about 150 ml of warm water, stirring for 10 min and diluting to volume in a 500-ml standard flask after cooling.

General procedure:
Place 10 ml of potassium dichromate stock solution in a 50-ml standard flask. Add 15.0 ml of 6M sulphuric acid and the appropriate amount of paracetamol solution. Swirl the flask and its contents and dilute to the mark. Place the flask in a water-bath maintained at 80° and leave it there for 15 min. Cool under tap water, and measure the absorbance at 580 nm against a reagent blank treated similarly.
References: