Estimation and Characterization of Paracetamol in Different Types of drug samples

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Abstract:

Paracetamol (acetaminophen) is a common analgesic and antipyretic drug that is used for the relief of fever, headaches and other minor aches and pains. Their determination in pharmaceuticals is of paramount importance, since an overdose of paracetamol can cause fulminating hepatic necrosis and other toxic effects. Many analytical methodologies have been proposed for the determination of paracetamol. The aim of the present study is to evaluate and study the structure of paracetamol contents produced by different companies and try to compare between the local paracetamol and imported ones. A varous techniques were used to explore and compare the information about composition, texture and structure. Drug samples were characterized by techniques such as scanning electron microscopy SEM, EDX, X-ray powder diffraction, UV. -visible spectroscopy and infrared spectra FTIR.

1. Introduction

Paracetamol (acetaminophen, N-acetyl-*p*-aminophenol) is one of the most widely used over-the-counter analgesic antipyretic drugs.[1] In 1877, aniline, a compound derived from coal tar, was discovered as a potential analgesic and antipyretic agent. In 1886, a chemist named Harmon Northrop Morse synthesized a derivative of aniline called para-aminophenol.[2] In 1893, while researching coal tar derivatives, Joseph von Mering and his colleague discovered that para-aminophenol could be used as a therapeutic agent.[3] However, because of the serious side effects associated with phenacetin such as hemolytic anemia and methemoglobin formation, its clinical use declined, and attention focused on paracetamol, which was marketed in 1893.[1] Additionally, more studies on phenacetin in the 1940s showed that paracetamol is one of its major metabolites and thus its pharmacological effects are attributed to paracetamol. As a result, paracetamol became freely available from the 1950s and has become the most widely used over-the-counter non-narcotic analgesic agent for the treatment of

mild to moderate pain and fever. Paracetamol (acetaminophen) is one of the most popular and widely used drugs for the treatment of pain and fever. Paracetamol offers several benefits, making it one of the most popular pain relief medications like effective pain relief,[4] fever reduction, gentler on the Stomach,[5] widely available,[6] safe for most populations,[7]….etc. Less Likely to Interact with Other Medications, paracetamol has fewer drug interactions compared to NSAIDs, making it a safer option for individuals on multiple medications.[8] It occupies a unique position among analgesic drugs.[9] Unlike NSAIDs it is almost unanimously considered to have no anti-inflammatory activity and does not produce gastrointestinal damage or untoward cardiorenal effects.[10] Also, unlike opiates it is almost ineffective in intense pain and has no depressant effect on respiration.[11] In this study we compared between locally manufactured paracetamol and well-known brands. The composition, structure and texture have been studied.

2. Experimental part

Six paracetamol tablet samples were collected for this study. These samples were produced by 3 local companies and by 3 companies from 3 different countries. All the samples were purchased in local pharmacies or in hospitals. Depending on the company, they were dispensed either in their original packaging or as single blister packs. Each tablet contained 500 mg or 1000 mg of paracetamol and was different sizes, shapes or colours. According to the labelling of some drugs, the types of excipients differed insignificantly. The paracetamol tablets were very well grinded to fine powder by using mortar, then labelled from Ay1to Ay6

3. Results and discussion:

3.1 Energy dispersive X-ray spectroscopy (EDX):

The elemental distribution on the surface of tablets was investigated using EDX while surface analysis to characterize the morphology of tablets was evaluated

using SEM at a nominal magnification of 1000 (area = 0.127 mm 0.095 mm) magnification. The detection of nitrogen (N) in phase (a) is characteristic of PMOL since this is the only N-containing component in the tablet formulations (Table 1).

Table 1: Composition of tablet samples.

Element	Atomic %					
	Ay1	Ay2	Ay3	Ay4	Ay5	Ay6
C	62.6	62.8	67.1	70.3	63.8	69.3
N	7.2	6.2	----	----	7.1	----
O	28.2	30.3	30.8	29.5	28.8	28.6
Mg	0.7	0.7	0.4	----	----	0.4
Si	0.9	0.8	0.7	----	----	1.0
Cu	0.4	0.3	0.7	0.2	0.3	0.4
Ni	----	----	0.4	----	----	0.2

However, the detected level of oxygen atoms is higher than expected suggesting that phase (a) is a combination of PMOL and C-888 as a result of the hot-melt extrusion processing. The EDX spectrum of phase-b showed the presence of C atoms although DCPA does not contain carbon. This was attributed to the close proximity of C-888 adjacent C-rich phases, particularly since the larger carbon signal in phase (b) is detected in batch-B where the homogeneity is higher. Phase (c) only contains C and O and hence it represents a mixture of sorbitol and C-888. In order to test the validity of the method of representing phases by spectra two approaches were used; one uses the percentage area of each phase and the second uses a semiquantitative elemental X-ray analysis of a wide area. The data in Table 1 shows the areas of the six phases, expressed as percentages of the total area examined, from an average of fifteen sub-sampled areas. The results from both batches are close to the initial proportions of the formulation ingredients. There is a greater deviation from the initial proportions in batch-A, which can be explained by the inferior drug/excipient homogeneity.

3.2 X-ray Diffraction (XRD):

Figures 1 and 2 present polycrystalline diffraction patterns of drugs Ay1 and Ay2 containing paracetamol. In all diffraction patterns, diffraction lines characteristic for ACP ($C_8H_9NO_2$) are present.[12] The position of the diffraction lines (2θ angles) and their intensities for the two Paracetamol are same, and there are on significant defferances between them.

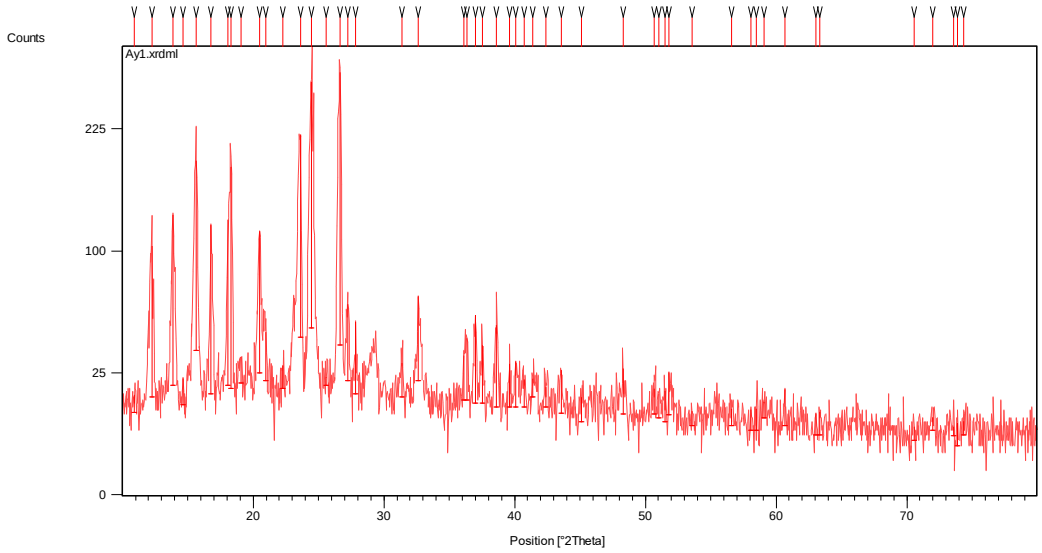

Figure 1: The XRD spectra of Ay1 paracetamol particles

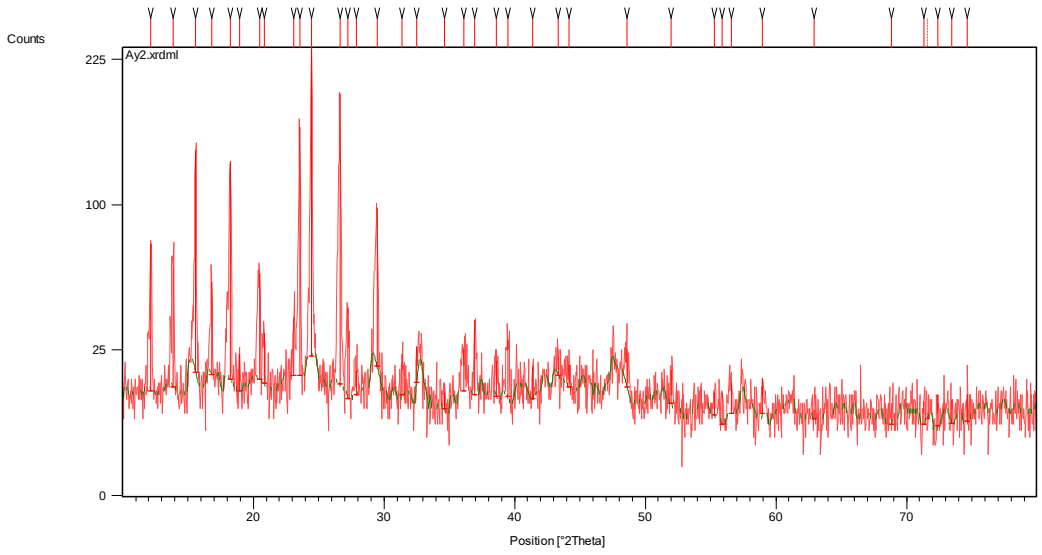

Figure 1: The XRD spectra of Ay 2 paracetamol particles

3.3 Fourier-transform infrared (FTIR):

The spectra of aqueous paracetamol solution in the range 1100-1800 cm-1 (Figure 2) were used to build a calibration model which relates the IR spectra to solution concentration. The absorbance in this region increased with concentration and temperature. The IR peak assignments of paracetamol in aqueous solution at room temperature are given previously.35 Because of the low solubility of paracetamol in water, the contribution of noise becomes significant and obtaining an accurate solution concentration measurement is challenging. Hence an advanced chemometric approach was used since it can produce calibration models that are an order-of-magnitude more accurate than methods based on absorbances at peaks.20,21 The regression coefficients for the calibration model (see Figure 3) show a broad peak at 1250 cm-1, indicating that the absorbances at these frequencies show a consistent positive correlation with the concentration of paracetamol in aqueous solution. This should not be surprising since this portion of the spectra is the least noisy (see Figure 2). There is a high positive correlation between the solution concentration and the absorbance at 1514 cm-1.The correlations between the solution concentration and the absorbances in the broad peak at 1575 cm-1 (see Figure 4) are much smaller than for the peaks at 1514 and 1250 cm-1. A significant advantage of using chemometrics to construct the

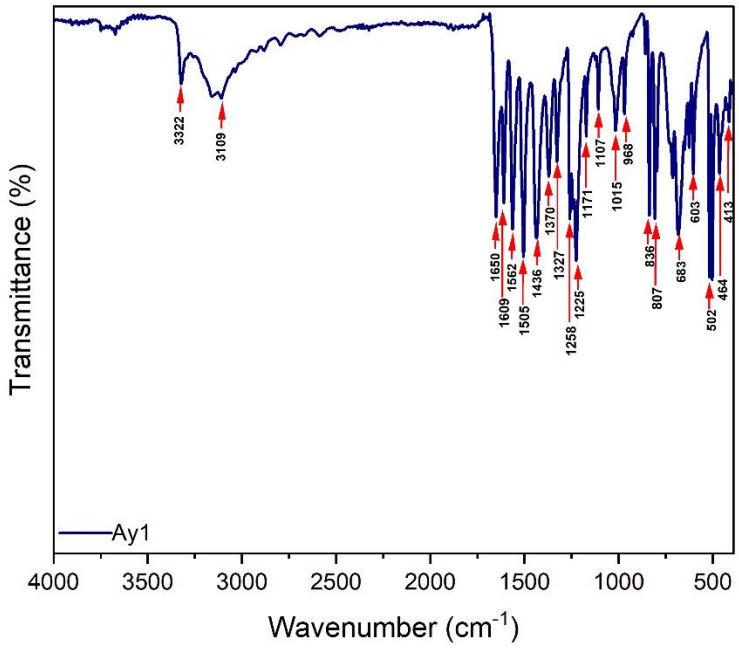

Figure 3: FTIR for Ay1 sample

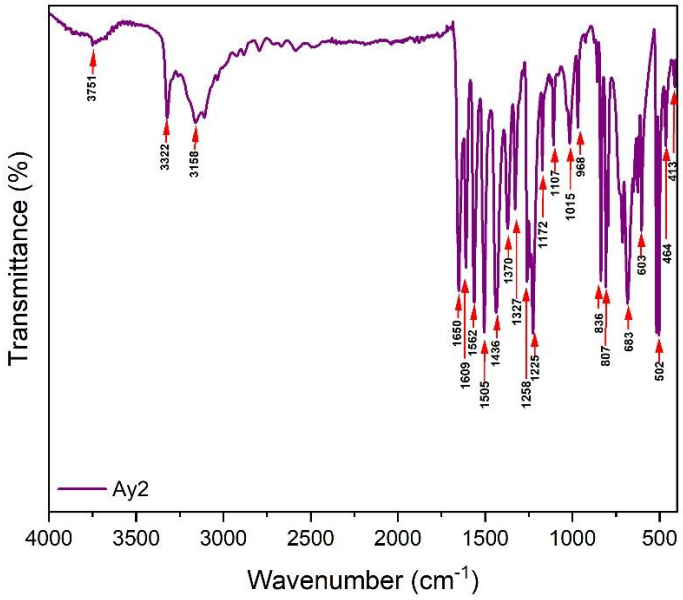

Figure 3: FTIR for Ay2 sample

Conclusion

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