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VALIDATION OF A UV-SPECTROPHOTOMETRIC METHOD FOR THE ASSAY AND PURITY OF PARACETAMOL IN SOLUTIONS FOR IV INFUSION, AND COMPARISON OF MARKETED BRANDS

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ABSTRACT

Paracetamol or chemically named p-acetyl-N-aminophenol is a unique analgesic and antipyretic widely used in the hospital setting all over the globe. The Paracetamol solution for IV infusion is clinically the standard analgesic in Pain Management and the first line, most safe antipyretic especially in the Pediatrics Department. According to many pharmacopoeias, the UV spectroscopy is still one of the most validated and relied on quality control assays in pharmaceutical research. Our research objective is to compare the purity and quantity of the Active Pharmaceutical Ingredient (API) "Paracetamol" in five different brands of Paracetamol solution for IV infusion present in the Lebanese market. The λmax was 244nm in all five brands which confirms purity of the API, however Amax was the highest in Bofalgan (Bosch Pharma) and lowest in Perfumol (Hikma Pharmaceuticals). The highest concentration was observed in Perfalgan (Bristol Myers Squibb), while the lowest concentration was observed in Perfumol (Hikma Pharmaceuticals).

Keywords: Paracetamol, Uv, Perfalgan, Bofalgan, Perfumol, Payal, Panpharma, Tabbouche Omar

INTRODUCTION

Paracetamol is a centrally acting analgesic/antipyretic with weak peripheral anti-inflammatory activity. Paracetamol is available in many pharmaceutical dosage forms like tablets, suspensions, elixirs, suppositories, and solutions for IV infusion. In the hospital setting, Paracetamol solution for IV infusion plays a central role in the management of mild to moderate post-operative pain, trauma pain, and fever, especially when other routes of administration are not applicable like in NPO patients, infants, children, or even when a rapid response is required. The UV assay of Paracetamol in various dosage forms has been described in numerous previous articles, and is a validated method for the measurement of purity and quantity endorsed by the leading Pharmacopoeial compendia around the world [1,2,3]. However, no previous article in the scientific literature has described the assay of Paracetamol in the injectable

form, or even made a comparison between the qualities of different injectable Paracetamol brands. To estimate Paracetamol in pharmaceutical dosage forms, UV-spectrophotometric and RP-HPLC showed no significant difference in accuracy, precision, and robustness [4]. The aim of our study is to publish a validated method for the estimation of Paracetamol in the injectable form, and to compare the quality and quantity of Paracetamol in different brands present in different markets around the world.

MATERIALS AND METHODS

Instrumentation: All experiments were conducted using Genesys 10S UV-Vis Spectrophotometer (Thermo Scientific™) and 1cm Quartz cuvettes.

Stock solutions of Paracetamol [5,6,7]: All injectable Paracetamol brands have the same concentration and volume of 10mg/ml & 100ml respectively. 25 ml

were pipetted from the bottle, and then transferred into a 250ml volumetric flask, and distilled water was added to get a 1mg/ml concentration.

Working solutions of Paracetamol: Five different dilutions (12.5, 25, 50, 75, & 100 μg/ml) were prepared from the stock solution by pipetting and transferring into 25ml volumetric flasks, then completing to the mark with distilled water.

Sample solutions: Our sample solutions included five bottles of injectable Paracetamol formulation from five different brands: Perfalgan (BMS-Lot Nb: 2A73072), Bofalgan (Bosch Pharma – Lot Nb: B0061), Perfumol (Hikma Pharmaceuticals – Lot Nb: 5269), Paracetamol Panpharma (Panpharma – Lot Nb: P111241D), Paracetamol Payal (Payal – Lot Nb: 110504).

UV Spectroscopy: A standard slope for each brand was built using the five different concentrations mentioned above. Absorbance scanning was conducted by measuring the Absorbance values at wavelengths ranging from 200nm to 350nm. Finally, Amax (λmax=244nm) was measured from the 12.5μg/ml and 25μg/ml dilutions which showed good linearity on the standard slope. Then the concentrations were calculated according to the following equations[8]:
- Quantity of Paracetamol in the sample = Standard sample weight (mg) xA_{244} (test) / A_{244} (std)
- Percentage assay of Paracetamol in the sample = 100 x calculated weight in sample / weight of sample

Statistics: The comparison of various parameters was conducted to elaborate the significant difference using software, SPSS version 13.0. The level of significance was set at 0.05.

RESULTS

The standard slopes showed good linearity between 12.5 μg/ml & 50 μg/ml. Standard slopes of the different brands were drawn on the same graph to compare linearity (Fig.1). To measure the purity of the API in the five different brands, absorbance scanning at wavelengths ranging from 200nm to 350nm was conducted (Fig.2). Quantification of the four different brands was calculated as a percentage of quantity compared to the standard branded drug "Perfalgan". Absorbances were measured on the 12.5, 25, & 50μg/ml dilutions that showed the best linearity on the standard slope. To ensure precision of our results, we tested our samples on a triplicate

basis, and calculated the mean value. Results are summarized in Table 1. The mean quantitation percentages of the four different brands compared to "Perfalgan" are summarized in Table 2.

DISCUSSION

Standard slope: The standard slope showed linearity up to the concentration of 50μg/ml. However, if we check the quantitative results, we can conclude that linearity is lost even before 50μg/ml. All of the five brands showed similar linearity slopes with the diluted solutions, whereas, at higher concentrations, linearity was most lost with Bofalgan. We can conclude that all brands showed a similar linearity profile with non-significant changes of absorbance value differences.

UV Spectrum: The UV spectrum shows us the absorbance values over varying wavelengths 1nm apart, ranging from 200nm to 350nm. All of the five brands showed the same peak at a wavelength of 244nm (λmax). They also shared a similar spectral pathway throughout the whole wavelength range. However, absorbance values did change at λmax which is of concern for us because it represents the peak absorptive value of Paracetamol according to Pharmacopoeias. The brands with the highest to lowest peaks are listed respectively as follows: Bofalgan, Perfalgan, Payal, Panpharma and Perfumol.

Quantitation: As described in Table 1 and Table 2, the percentage values differed between different concentrations, the most significant values being at the 12.5 & 25μg/ml. At the concentration of 50μg/ml, linearity was lost, hence, the quantitative results are not statistically significant. The mean percentages of the four brands at the 12.5 & 25μg/ml concentrations are more statistically significant. The brands showing the highest to the lowest concentration of Paracetamol are listed respectively as compared to the branded product "Perfalgan": Boflagan, Payal, Panpharma, and Perfumol. All brands have percentages above 80% which means that they all are accepted as generics according to the FDA generics rule, but they do differ in the concentrations found, hence, we do have brands with better quality over others. To summarize the quality results of the four different brands as compared to Perfalgan, the best generic is Bofalgan, while the worst is Perfumol. Paracetamol Payal & Paracetamol Panpharma come in the second and third position respectively.
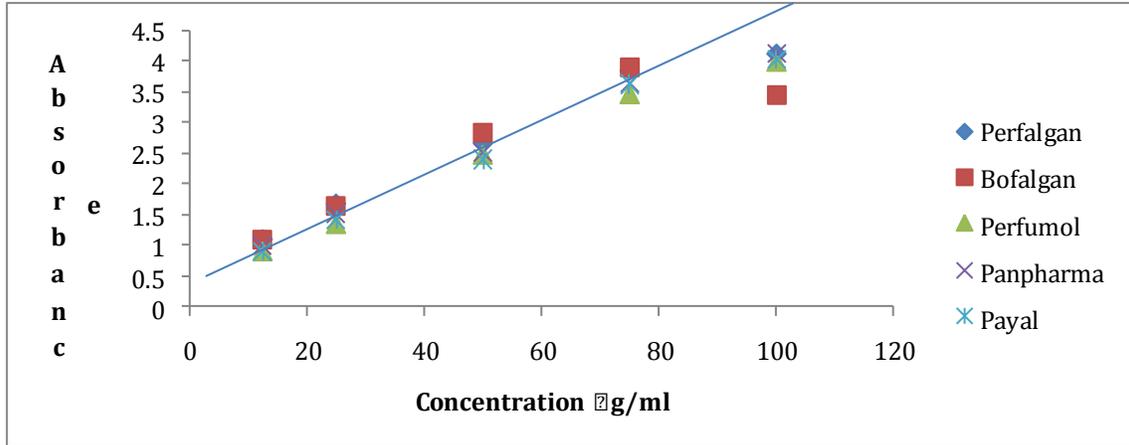
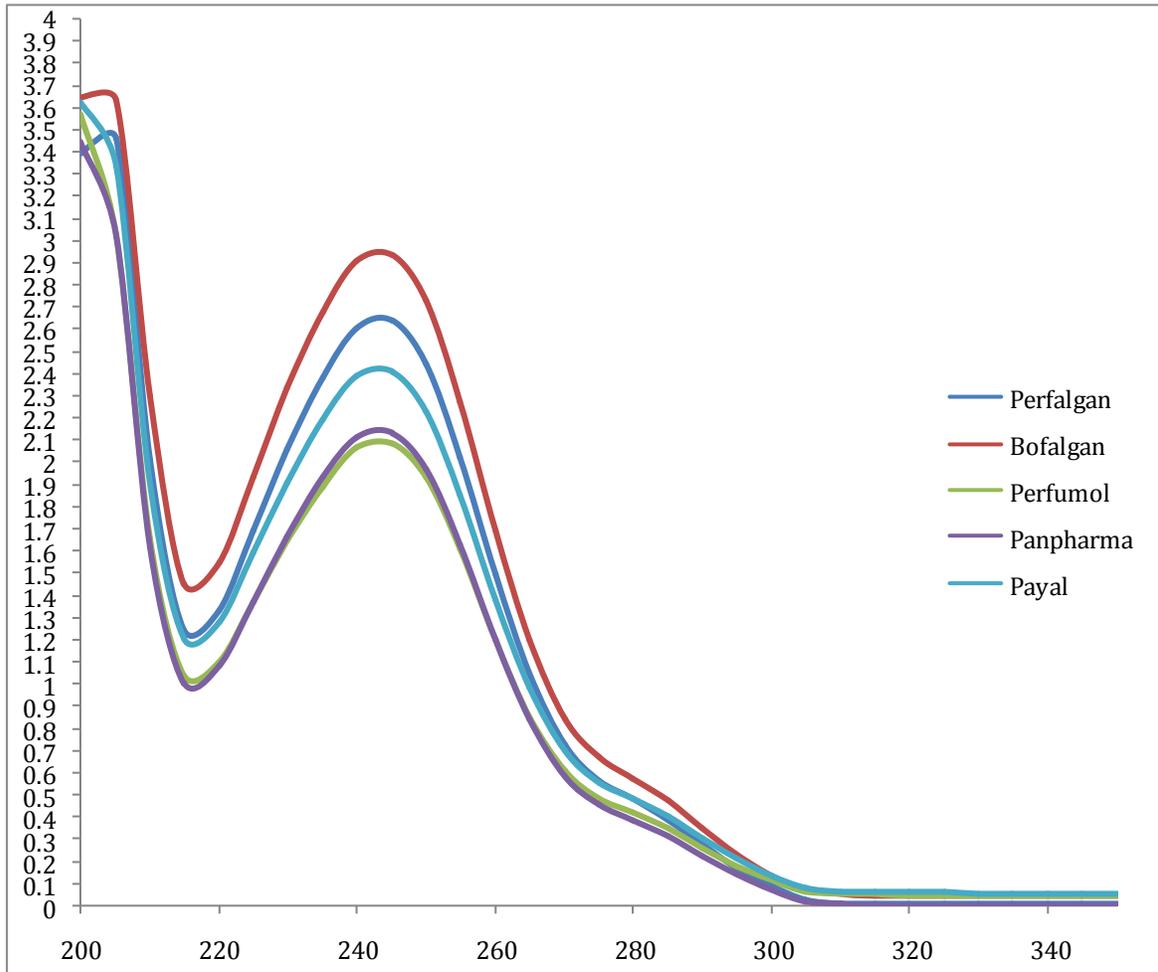Fig.1 Standard slopes of the five brands measured at 244 nm.

Fig.2 Scanning graph of the five different brands at 25 μg/ml & 50 μg/ml showing λmax at 244 nm.
Highest peak corresponds to Bofalgan, while the lowest peak corresponds to Perfumol

Table 1: Absorbances and quantitation percentages of the four different brands in relation to the branded product "Perfalgan"

C_{Std}	A_{std}	$A_{Bofalgan}$	$\%_{Bofalgan}$	$A_{Perfumol}$	$\%_{Perfumol}$	$A_{Panpharma}$	$\%_{Panpharma}$	A_{Payal}	$\%_{Payal}$
12.5	1.087	1.057	97.24	0.843	77.55	0.887	81.60	0.873	94.89
25	1.671	1.554	92.99	1.327	79.41	1.352	80.90	1.315	78.69
50	2.665	2.906	109	2.296	86.15	2.329	87.39	2.424	90.95

Table 2: Mean quantitation percentages of the four different brands

Product	Quantity % (including 50µg/ml)	Quantity % (excluding 50µg/ml)
Bofalgan	99.74	95.11
Perfumol	81.03	78.48
Panpharma	83.29	81.25
Payal	88.17	86.79

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