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## **A Review on Colorimetric Determinations of Paracetamol by Spectrophotometry**

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### **ABSTRACT:**

The colorimetric determinations of Paracetamol in the bulk and pharmaceutical dosage form were carried out with different colouring reagents. The production of a coloured solution served as the foundation for the techniques. The qualitative or quantitative determination is based on the colour formation reactions of Paracetamol with colouring reagents. The wavelengths ( $\lambda_{max}$ ) were used 430,450,468,505,528,60 6,635,640,650 and 715nm. The calibration curves were constructed from the concentrations ranging from 0.1- 100  $\mu$ g/mL and regression coefficient values were found to be  $>0.998$ . The % RSD values of the precision were found to be  $<2$ . The methods were more accurate and values were found in between 99-101%. The methods were shown good robustness values and % RSD values were found to be  $<2$ .

**KEY WORDS:** Paracetamol, Colorimetric method, Colouring reagents

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### **INTRODUCTION**

Paracetamol (figure-1) is an analgesic and antipyretic<sup>1</sup>. Numerous spectrophotometric techniques have been documented for determining paracetamol, formed the red dye with diazotized 4-nitroaniline (DNAN) in sodium carbonate medium<sup>1</sup>, majority of published methods were on hydrolysis of the compounds leading to the Schiff base formed with a substituted benzaldehyde<sup>2</sup>, reaction of sodium nitrite with drug forms the diazonium salt and coupling reagent was 1-Naphthol<sup>3</sup>, 2,4,6-trimethoxybenzaldehyde coupling formed pink colour<sup>2</sup>, the drug forms the colour with p-dimethyl amino benzaldehyde in the 95% ethanol and 2M HCl<sup>5</sup>, estimation of drug in plasma with sodium nitrite, one of the most often

used Cl reagents is luminol<sup>6</sup>. Several oxidizing chemicals, including permanganate (MnO<sub>4</sub>-2), oxidize it, hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>), periodate (IO<sub>4</sub>-2), and hypochlorite (ClO-).

Luminol undergoes oxidation to yield 3-aminophthalate, an excited state product that emits blue light with a maximum wavelength of 425 nm. Additionally, diperiodatocuprate (III) (DPC), diperidoatonicluate (IV) (DPN), and diperidodatoargentate (III) (DPA) are among the other high and unusual oxidation state transition metal complexes that are being used more and more for analytical purposes<sup>7</sup>. Microwave assisted hydrolysis of paracetamol with 2,2-(1,4-phenylenedivinylene) bis-8-hydroxyquinoline<sup>8</sup>, the colorimetric reagents Fe<sup>+3</sup> and K<sub>3</sub>[Fe(CN)<sub>6</sub>] were employed for the determination of compound with exhaled breath

condensate technique (EBC),  $\text{Fe}^{+3}$  reduced to  $\text{Fe}^{+2}$  and  $\text{K}_3[\text{Fe}(\text{CN})_6]$  chelated the  $\text{Fe}^{+2}$  9 , oxidative coupling reaction of para amino phenol with p-xylenol (2,5-diethylphenol)10, reduce the compound with ceric ammonium sulphate11, the process produces a prussian blue (PB) complex by oxidizing paracetamol with  $\text{Fe}(\text{III})$  and then reacting with ferricyanide in the presence of  $\text{HCl}$ 12 , charge transfer complex formed between chromogenic reagent of chlorferone with drug13, oxidative coupling reaction of paracetamol with phenylephrine hydrochloride in ambient oxygen and in an alkaline media, produce a stable, water-soluble indophenol dye14, coupled reaction of 1-naphthol15, indirect determination of paracetamol with Luminol- $\text{H}_2\text{O}_2$ - $\text{Fe}(\text{CN})_3$ 17 and based on the oxidation between drug and  $\text{Fe}(\text{CN})_3$ 6, it prevents reaction between luminol and hydrogen peroxide18.

The analyte oxidised with  $\text{K}_3[\text{Fe}(\text{CN})_6]$  at ambient temperature in ammonical aqueous solution by using anionic ion exchange column in the flow injection-spectrophotometric method19,20, talkaline hydrolysis of the analyte formed blue indophenol dye with 8-quinolinol in presence of  $\text{KIO}_4$ 21-25, reaction with 2-nitroso-1-naphthol-4-sulfonic acid26, Stable colour complex produced with a Folin-Ciocalteau reagent27, formation of 2-nitro-5-acetamidophenol derivative with nitrous acid in an alkaline medium28.intrusion of salicylates and salicylamide in the colorimetric.

Nitration method and grieves the estimation of paracetamol29,based on ring-nitration of the drug30, using chlorferone31, using  $\text{ZrO}_2$  (IV) and  $\text{NH}_4\text{NO}_3$  (V)32 ,Colorimetric method of Glynn and Kendal 33, reduction of tris(2,2'-bipyridyl) ruthenium(III)34, luminol-permanganate based reaction35, using N, N-dibromo dimethylhydantoin36, 4-(Dimethylamino)benzaldehyde react with N-(4-hydroxyphenyl)ethanamide in 2M  $\text{HCl}$  after heating37, fluorophore heroin reagent was used with  $\text{NaClO}$  oxidizing agent and pH was optimized at 10 with borate buffer38.

$\text{NaClO}$  oxidizes the analyte and excess of the oxidant determined with o-tolidine dichloride as chromogenic reagent at 430 nm 39.Paracetamol was dissolved in 4M sulphuric acid and treated with 10.0 mg of sodium bismuthate in the presence of 1M  $\text{HCl}$  and 1M acetic Acid. It exhibited a stable bluish-violet colour40. Paracetamol to p-aminophenol that reacts with  $\text{S}^{2-}$  in the presence of  $\text{Fe}^{3+}$  as oxidant to create a dye that resembles methylene blue and has an  $\lambda_{\text{max}}$  at 540 nm41.The N-(4-hydroxyphenyl) ethanamide on the hydrolysis formed p-aminophenol and oxidant is dissolved oxygen in the alkaline medium, further formed in to N-acetyl-p-benzoquinone imine, which is capable to produce green indophenol dye with tiron42, estimate the drug by using cadmium pentacyanonitrosylferrate modified glassy carbon electrod43,  $\text{Fe}^{+3}$  ions oxidize paracetamol and salicylamide when 1,10-phenanthroline is present44.,

## MATERIAL & METHODS

The materials were used in the colorimetric methods paracetamol, diazitized 4-nitroaniline1,  $\text{HCl}$ , benzaldehyde,  $\text{Na}_2\text{CO}_3$ , 2,4,6-trimethoxybenzaldehyde2, resorcinol, ammonium sulfamate3, sodiumnitrite, 1-Naphthol3,4,6, 4-amino phenol,  $\text{Na}_2\text{SO}_4$ , tetrahydroxycalix, indophenol dye4, dimethylamino benzaldehyde5, chloroacetic acid,  $\text{NaOH}$ , sulphamic acid,ethanol, luminol,  $\text{KMnO}_4$ ,  $\text{H}_2\text{O}_2$ ,  $\text{KOH}$ 7, diperidodatoargentate (III)7,  $\text{K}_3[\text{Fe}(\text{CN})_6]$ ,  $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}_9$ , sodium periodate, tylenol10, ascorbic acid, phenylephrine hydrochloride, 2,6-dichloro indophenol, n-polopiryna11, styrene, maleic anhydride, benzoyl peroxide, tetrahydro furan, diethyl ether, acetonitrile, poly (styrene-alt-maleic acid), methanol12, 2,2-(1,4-phenylene divinylene) bis-8-hydroxyquinoline, ferric chloride, p-xylenol (2,5-diethylphenol), potassium ferricyanide12,16, protrolyptiline  $\text{HCl}$ , chlorferone13,14,31, ceric ammonium sulphate13, Iron (III)15, Zirconium (IV) oxide, ammonium trioxovanadate (V)32, N,N-Dibromo dimethylhydantoin36, O-tolidine39, Cadmium Pentacyanonitrosylferrate43.

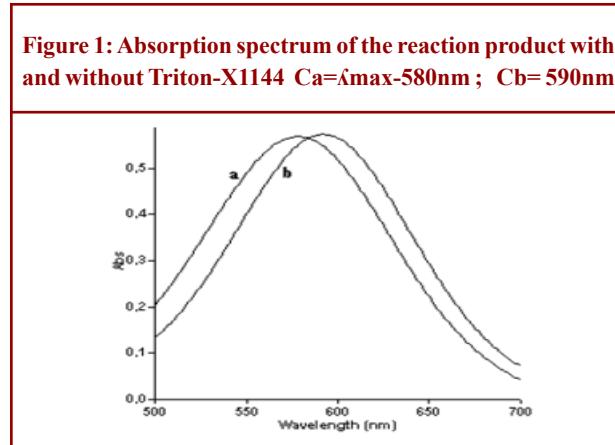
**Preparation of sample solutions:** The majority of published methods were reported the preparation sample solutions depends on acid hydrolysis of the paracetamol with substituted benzaldehyde forms the Schiff base2, microwave assisted hydrolysis4, few methods have been reported on coupling reactions with coupling reagents2, oxidation of the drug with oxidizing agents and oxidation state transition metal complexes and formation of charge transfer complexes7.

## RESULTS & DISCUSSION

The created procedures were validated in accordance with several recommendations, and the results produced fell within the acceptable range. The reported methods were shown good linearity and regression coefficient values were found to be greater than 0.999. The linearity range were found to be 0.5-20  $\mu\text{g/mL}$ 1 for batch method 1-150  $\mu\text{g/mL}$  for FI method1, 20-100  $\mu\text{g/mL}$ 2, 2-10  $\mu\text{g/mL}$ 3, 1.5-12  $\mu\text{g/mL}$  for conventional UV method for cloud point extraction technique the linearity range reduced to 0.14 - 1.5  $\mu\text{g/mL}$ 4 (figure-2), 1-5 mg/mL5, 25-400 mg/L6, 0.075-0.75 mg/L7, 0.44-5.5 mg/L8, 0.2-10  $\mu\text{g/mL}$ 9, 25-600  $\mu\text{g/mL}$ 10, 0.01-0.5  $\mu\text{g/mL}$ 12, 40-160  $\mu\text{g/mL}$ 13, 50-500 mg/L28, 0.5-24  $\mu\text{g/mL}$ 14, 2-10  $\mu\text{g/mL}$ 15, 0.1- 2.4  $\mu\text{g/mL}$ 16, 2-16 mg/mL17.

The %RSD of the accuracy obtained results were found to be within the limits as per guidelines. The concentration ranges of the reported methods were found to be from 0-60 mg/ml, 0.8 – 3.36 mL, 0 to 10  $\mu\text{g/ml}$ , 0.01 – 0.70, 1.5—12 mg/mL, 0.075-0.75 mg/L, 0.2-10.0  $\mu\text{g/mL}$ , 2.5-25  $\mu\text{g/mL}$  and >70  $\mu\text{g/mL}$ , 25 to 60 mg/ml, 0.25-30 ppm19, 0.2-20 ppm20, f 0.01-0.5 mg/mL, 10.00-60.00 g/mL, 0.5-24  $\mu\text{g/mL}$ , 2 – 10  $\mu\text{g/mL}$ , 1.0-3.0 mL. The reported values were found the good LOD & the lowest LOD is 0.0369  $\mu\text{g/mL}$  whereas the highest LOD is 40.0 mg/mL. The various methods have been reported and

values were found to be 40.0 mg/mL, 0.0007 mg/mL, 0.2  $\mu$ g/mL, 0.49  $\mu$ g/mL, 0.007  $\mu$ g/mL, 0.0578  $\mu$ g/mL, 0.02 g/mL, 0.03 g/mL, 0.0448 mg/mL.



The quantification limit values were found to be 0.002 mg/L, 0.166 mg/mL, 0.1753 g/mL, 0.10 g/mL, 0.08 mg/mL, 0.149 mg/mL, 0.121 mg/mL. The %RSD values of robustness were found to be within the limits as per guidelines. The review article focused on the colourimetric determination of paracetamol with different colouring reagents and validation parameters. The Hayati filik et al<sup>4</sup> reported lowest linearity concentration range from 0.14-1.5  $\mu$ g/mL with CPE method by using with colourant calixarene (CAL4) in the presence of KIO<sub>4</sub> oxidant and colour of the solution was blue. Cloud point phase separation was done with Triton X-114 (surfactant micelles) by addition of Na<sub>2</sub>SO<sub>4</sub>. It is the high sensitive method because of detection limit was found to be 40ng/mL.<sup>4</sup>

Paracetamol estimated in urine by using different colouring reagents and their linearity concentration values were reported in table 1.

**Table:1 Colorimetric estimation of Paracetamol in Urine<sup>4</sup>**

Method	Linearity range ( $\mu$ g/mL)	LOD (ng/mL)	Reference
Phenol	100-800	NR	Welch et al <sup>47</sup>
o-Cresol	0.3-12	100	Criado et al <sup>45</sup>
Xylenol	20-400	NR	Chen et al <sup>49</sup>
Resorcinol	2-100	900	Bocxlaer et al <sup>48</sup>
8-hydroxyquinoline	0-2.5	NR	Morris et al <sup>50</sup>
Derivative UV	5-30	2000	Parojicic et al <sup>51</sup>
Diazotisation	2-10	NR	Heirwegh et al <sup>46</sup>
ELSD	1-100	300	Criado et al <sup>52</sup>
UV-Visible	1.5-12	500	Hayati Filik et al <sup>4</sup>
CPE-UV-Visible	0.14-1.5	40	Hayati Filik et al <sup>4</sup>

## CONCLUSION

The paracetamol was estimated colorimetrically by using spectrophotometer with different coloring reagents. The charge transfer complex formed between chromogenic reagent of chlorferone with drug and shown sensitivity of the method. Different oxidation reactions were carried with oxidizing (coupling) agents were used with alkaline or acidic medium and produces the more intense colour, determined in visible range. The colourant calixarene (CAL4) in the presence of KIO<sub>4</sub> oxidant the drug was produced blue colour. This reagent used for the estimation of drug in the urine, with cloud point phase separation Triton X-114 (surfactant micelles) was used by addition of Na<sub>2</sub>SO<sub>4</sub>. It is the high sensitive method because of LOD was found to be 40 ng/mL and linearity range was found to be 0.14-1.5  $\mu$ g/mL.

The drug produces the stable colored complex with Folin-Ciocalteau reagent it enhance the sensitivity and stability of the method. The other colorants were used benzoyl peroxidepoly (styrene-alt-maleic acid), 2,2-(1,4-phenylene divinylene) bis-8-hydroxyquinoline, ferric chloride, P-xylenol (2,5-diethylphenol), potassium ferricyanide<sup>12,16</sup>, protryliptyline HCl, chlorferone<sup>13,14,31</sup>, ceric ammonium sulphate<sup>13</sup>, Iron (III)<sup>15</sup>, Zirconium (IV) oxide, ammonium trioxovanadate (V)<sup>32</sup>, N,N-Dibromo dimethylhydantoin<sup>36</sup>, O-tolidine<sup>39</sup>, Cadmium Pentacyanonitrosylferrate<sup>43</sup>.

**Conflict of Interest:** The authors have stated that they don't have any conflicting interests.

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