Simple Analysis Used in Diagnosis and Follow-up of Schizophrenic Patients

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Dopamine acts as neurotransmitter in the central and peripheral sympathetic nervous system. Determination of dopamine (DO) was performed by spectrophotometric analysis depending on the formation of new colored compound. The proposed procedure was efficient in quantitative determination of DO as pure material in pharmaceutical preparations and in urine samples. DO concentration in urine sample of patient confirms the affection with schizophrenia and the proposed procedure was used to facilitate diagnosis and followup of schizophrenic patients. It is recommended to apply the proposed procedures as routine analysis in pharmaceutical companies for quality control and in analytical laboratories to diagnose and follow up schizophrenia.

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1. INTRODUCTION

Dopamine and dopamine derivatives were a group of biogenic amines possessing a 3,4-dihydroxy substituted phenyl ring (Figure 1). They are considered as a type of hormones widely spread in animals and had also been detected in 44 plant families [1, 2]. They also seemed to be a central pharmacophore and well probably existed in future drugs, especially in those developed for psychiatry disorders and neurological activity [3]. It was not until the late 1950s that dopamine was recognized as a mammalian neurotransmitter in its own right but the demonstration of its nonuniform distribution in the brain suggested that it might has a specific functional role for dopamine [4]. It had therapeutic uses as a cardiostimulant and had important role in the pathogenesis or drug treatment of certain brain diseases, for example, Parkinson’s disease and schizophrenia [5].

Several methods were applied on pharmaceutical preparations containing DO.HCl or LD depending on oxidation reaction [6–8]. Determination of certain catechol derivatives like pyrocatechol, DO.HCl, and LD in either pure form or in its pharmaceutical formulation was suggested spectrophotometrically [9–11] and indirect kinetic spectrophotometry [12].

HPLC technique is most predominantly used for screening of many clinical diagnosis [13–15] and to find the difference between the measured and ordered doses of catecholamine infusion [16]. Flow injection analysis (FIA) system using tubular electrode was used in the determination of DO in pharmaceutical preparations. The process based on redox properties of copper (II) ions immobilized in a poly (ethylene-co-vinyl acetate) (EVA) membrane and oxidation of DO [17].

In continuation to our interest in microdetermination of these drugs under study [18], the aim of the present work is to describe the development of simple, sensitive, and rapid spectrophotometric method for the determination of DO.HCl depending on the formation of coloured complex between DO and copper sulfate and 4-amonoantipyrine (4-AAP). Different experimental conditions are carefully studied before applying Beer’s law. The method was applied for determining DO in urine samples collected from schizophrenic patients and pharmaceutical forms. The results obtained are of interest and are compared with these obtained by the official method.

2. EXPERIMENTAL

2.1. Procedure

An aliquot containing 74.4–417.2 ppm of DO.HCl was transferred to 10 mL measuring flask, followed by adding 4-AAP and copper sulfate. The pH was adjusted at 10-11. The total volume was completed up to 10 mL. The mixtures were
was obvious that the most suitable pH is 10-11 for microde-
type compounds involved [19–21].

2.3. Analysis of DO in urine samples of healthy
individuals and schizophrenic patients

Urine samples were allowed to stand at room temperature
before pipetting. To be sure of complete homogeneity, a rapid
vortex must be done for 30 seconds.

Certain volume from urine sample was mixed with 4-
AAP and copper sulfate at pH 10-11. The total volume was
completed up to 10 mL measuring flask using deionized wa-
ter. The method was completed under optimum conditions.

From the calibration curve, the concentration of dopam-
ine in different urine samples can be calculated.

2.4. Results and discussion

4-AAP reacts with phenolic-type compounds according to
the reaction shows in Figure 2. The reaction product may be
of any color from red to purple depending on the phenolic-
type compounds involved [19–21].

Optimum conditions affecting the reaction of DO.HCl
with copper sulfate and 4-AAP were studied carefully. The ef-
effect of pH was studied in the pH ranging from 9 to 12 and it
was obvious that the most suitable pH is 10-11 for microde-
termination of DO.HCl at \( \lambda_{\text{max}} = 480 \text{ nm} \).

Applying the molar ratio method, it was found that
DO.HCl interacts with 4-AAP and copper sulfate to form
product in ratio 2 : 2 : 1 as [DO] : [4-AAP] : [Cu\(^{2+}\)]. The
solid of this reaction is separated and characterized using dif-
ferent tools like elemental analysis, IR, magnetic and thermal
analysis. By following the reaction at different time intervals,
it is obvious that the suitable time needed for complete reac-
tion was 10–30 minutes which was attained at room temper-
ature.

Under the optimum conditions, a correlation was ob-
tained between absorbance (A) and the concentration (C)
over the range at 74.4–417.2 \( \mu \text{g mL}^{-1} \) of DO.HCl (as shown
in Figure 3). The apparent molar absorptivity, Sandell sen-
sitivity, standard deviation (SD), and coefficient of variation
(CV) for each active ingredient were tabulated in Table 1. The
apparent molar absorptivity (\( \epsilon \)) of the resulting col-
ored products was found to be 2.979 \( \times 10^{4} \text{ L mol}^{-1} \cdot \text{cm}^{-1} \),
whereas Sandell sensitivities were \( 3 \times 10^{-3} \text{ mg cm}^{-2} \). The cor-
relation coefficient was found to be 0.999, while the SD
was 0.06–0.3. The low values of CV and SD indicated the
high accuracy, precision, and reproducibility of the proposed
method to determine DO.HCl.

2.5. Interference

Several pharmaceutical preparations were associated with
flavoring agents, diluents, and excipients. The common toler-
ances, which were examined in our proposed procedure with
active ingredients DO.HCl, were glucose, acetone ascorbic
acid, urea catechol, phenol, pyrogallol, resorcinol, and hy-
droquinone as shown in Table 2.

3. APPLICATIONS

3.1. Determination of DO.HCl in pharmaceutical forms

Our proposed procedure was applied on ampoule containing
DO.HCl as active ingredient, as shown in Table 3. Detection
of DO.HCl concentration in aliquot solutions was applied
with percent error 0.3%. The percent error was very small
that could be neglected and was in acceptable range of error
for pharmaceutical determination [22, 23].

The calculated values of \( t \) and \( F \) tests [24] under con-
fidence limit 95% = 2.5–2.8 and 5.11–5.8, respectively, in-
dicated insignificant difference between the official [25] and
proposed methods and also referred to the robustness of the
proposed procedure.

3.2. Determination of DO in urine samples
of schizophrenic patients

Before our method, schizophrenia was diagnosed by physi-
cians clinically through an interview with the patient and
followed-up schizophrenic patients via clinical diagnosis.
Proper response and improvement appear clinically within
4–6 weeks from starting antipsychotic drugs [26].

In the treatment of schizophrenia, more than in many
other diseases, individual patients respond differently to
medication. Despite recent advances in the treatment of
schizophrenia, there remains a number of unmet needs in
therapy for schizophrenia management like low response,
high relapse rates [27–30], nonresponse [27, 30–37], nonad-
herence [27, 29] or challenging road ahead.

Nowadays with our new option, analytical test is ordered
after a psychiatrist performing his clinical examination [38]
on the patient and suspecting that patient has schizophrenic
symptoms [39]. Actually it can be used as a monitoring tool
to follow up a patient treatment and in confirming psychia-
trist findings. In addition, it can be applied before treatment,
after fifteen days from starting treatment and after thirty days from treatment. By this way, a psychiatrist will have facilities to evaluate the schizophrenic patient as a whole and to follow up the responsibility of the patient to recommended treatment according to the DO concentration present in urine sample. Moreover, it can be ordered as a routine analysis for early detection when a patient has a family history of schizophrenia.

### 3.3. Modification in spectrophotometric determination of DO in urine samples

The modification is based on formation of colored stripe sheet, which was picked from the calibration curve of DO.HCl with copper sulfate and 4-AAP under optimum conditions. The collected urine sample was mixed with copper sulfate and 4-AAP and allowed to stand under optimum conditions till complete complex formation, then the end colored product was compared with colors present in colored stripe sheet. By this way, we will have ability to detect the concentration of DO in the urine sample easily without the need to record absorbance at a certain wavelength using spectrophotometer.

So we can conclude that modification in our procedure facilitates quantitation of DO in urine sample without need to form calibration curve from time to time using standard DO material.

## 4. CONCLUSION

The proposed method and its modification for DO estimation were advantageous over many reported methods, where they facilitate quantitation of DO in urine samples without the need to form calibration curve from time to time using standard DO material. Moreover, early detection, diagnosis, followups and prevention of relapse of schizophrenic patients will be fast and easy.

This method could be used for the routine quality control analysis due to its sensitivity, rapidity, noninterference
Table 3: Determination of DO.HCl in pharmaceutical preparation using copper sulfate and 4-AAP reagents.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Name of preparation</th>
<th>Drug (ppm)</th>
<th>Recovery %</th>
<th>SD</th>
<th>*t test</th>
<th>F test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Taken</td>
<td>PM</td>
<td>OM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DO.HCl</td>
<td>Dopamine Fresenius</td>
<td>76.61</td>
<td>100.9</td>
<td>100.8</td>
<td>0.10</td>
<td>1.18</td>
</tr>
<tr>
<td></td>
<td></td>
<td>153.23</td>
<td>100.2</td>
<td>99.17</td>
<td>0.11</td>
<td>1.05</td>
</tr>
<tr>
<td></td>
<td>Dopamine Pierre Faba</td>
<td>76.61</td>
<td>101.8</td>
<td>102.2</td>
<td>0.17</td>
<td>1.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>153.23</td>
<td>100.2</td>
<td>101.1</td>
<td>0.13</td>
<td>1.5</td>
</tr>
</tbody>
</table>

* t test shows the values for V as degree of freedom for 95% confidence level (number of replicates v₁ = 5).
* F test shows the values for V as degree of freedom for variation confidence level (number of replicates v₁, v₂ = 5, 3).

with other ingredients usually present in pharmaceutical preparations, precision, and good agreement with the official method.

REFERENCES


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