The anodic oxidation of sulpha drugs (sulphanilamide and its derivatives) was carried out by several workers (190-192) at platinum and graphite electrodes using different electroanalytical techniques and conflicting results have been reported.

Voorhies and Adams (190) carried out the oxidation of sulpha drugs, at the platinum electrode, voltammetrically, in solutions of different pH values and reported the formation of a single anodic wave involving one electron change. Voorhies and Furman (191) studied the oxidation of these drugs chronopotentiometrically and observed that the oxidation process involved 2 electrons and not one. Bansal (192) investigated the oxidation of these drugs at the graphite electrode, using hydrodynamic voltammetry and observed the formation of a single anodic wave involving 2 electron change.

It is planned to carry out linear sweep voltammetric studies of these drugs, in well defined hydrodynamic systems, at the tubular graphite electrode with a view to confirm the already reported results under better experimental conditions and to suggest mechanism for their anodic oxidation. An attempt has also been made to use linear sweep voltammetry, in flowing solutions, for quantitative determination of these compounds in their pharmaceutical preparations.
ANODIC OXIDATION OF SULPHA DRUGS

Concn = $10^4$ M

$\nu_a = 1.0161 \text{ cm sec}^{-1}$

$\nu = 1.0 \text{ V min}^{-1}$

**FIG. 49**
Sulphanilamide

**FIG. 50**
Sulphadiazine

**FIG. 51**
Sulphaguanidine

**FIG. 52**
Sulphamethazine

Potential (V) vs SCE
Sulpha drugs, namely, sulphanilamide, sulphapyridine, sulphadiazine, sulphaguanidine, sulphamerazine, sulphathiazole and sulphamethazine were obtained from May and Baker Ltd., England, in pure form and used as such for voltammetric studies.

Voltammograms

Voltammograms for the oxidation of all sulpha drugs were recorded at a scan rate of $1.0 \text{ V min}^{-1}$ and velocity of $1.0161 \text{ cm sec}^{-1}$, in $0.1 \text{ M H}_2\text{SO}_4$. The voltammograms for four sulpha drugs namely sulphanilamide, sulphadiazine, sulphaguanidine and sulphamethazine are shown in figures 49-52. Since the behaviour of other sulpha drugs was found to be similar, their voltammograms have not been shown. Peak currents and half-peak potentials obtained in case of these drugs are shown in Table VI.

Discussion

During the first anodic scan all the sulpha drugs exhibit only a single well defined oxidation wave. The formation of single oxidation wave can be explained on the basis of E-E mechanism. According to this sulpha drugs during oxidation lose one electron to produce a cation radical which through its resonance structure undergoes head-to-head coupling resulting the formation of 4,4'-disulphonamido (-R) hydroazobenzene which undergoes oxidation at the same potential to form 4,4'-disulphonamido (-R)
Table VI: Anodic oxidation of sulpha drugs

General structure $\text{H}_2\text{N} = \text{SO}_2\text{NH} \ R$

<table>
<thead>
<tr>
<th>Compound</th>
<th>R</th>
<th>Half-peak potential $E_{p/2} (V)$ vs SCE</th>
<th>Peak current $i_p/\mu A$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Sulfanilamide</td>
<td>H</td>
<td>0.98</td>
<td>30.2</td>
</tr>
<tr>
<td>2. Sulfapyridine</td>
<td>$\begin{array}{c} \text{N} \ \text{NH} \end{array}$</td>
<td>0.95</td>
<td>29.8</td>
</tr>
<tr>
<td>3. Sulfadiazine</td>
<td>$\begin{array}{c} \text{N} \ \text{N} \end{array}$</td>
<td>1.00</td>
<td>29.6</td>
</tr>
<tr>
<td>4. Sulfaguanidine</td>
<td>$\begin{array}{c} \text{C} \ \text{NH} \end{array}$</td>
<td>0.97</td>
<td>29.9</td>
</tr>
<tr>
<td>5. Sulfamerazine</td>
<td>$\begin{array}{c} \text{N} \ \text{CH}_3 \end{array}$</td>
<td>0.96</td>
<td>28.4</td>
</tr>
<tr>
<td>6. Sulfamethazine</td>
<td>$\begin{array}{c} \text{N} \ \text{CH}_3 \ \text{CH}_3 \end{array}$</td>
<td>0.99</td>
<td>29.1</td>
</tr>
<tr>
<td>7. Sulfasomidine</td>
<td>$\begin{array}{c} \text{S} \ \text{CH}_3 \end{array}$</td>
<td>0.96</td>
<td>28.7</td>
</tr>
<tr>
<td>8. Sulfathiazole</td>
<td>$\begin{array}{c} \text{S} \end{array}$</td>
<td>0.98</td>
<td>29.2</td>
</tr>
</tbody>
</table>
azobenzene as a stable product. The possibility of head-to-tail and tail-to-tail coupling, is ruled out because para position in all cases is occupied. The reaction scheme is represented as

\[
\text{sulpha drug} \quad \text{NH}_2 \quad \text{SO}_2 \text{NHR} \quad \rightarrow \quad \text{mono cation radical} \quad \text{H-N-H} \quad +e^- \quad \text{SO}_2 \text{NHR} \quad \text{RHN</SO</HR>}
\]

Resonance structures of cation radical

**Head-to-head coupling**

\[
\text{RHN</SO</HR>NH}_2 \quad + \text{H</SO</HR>NH}_2 \quad \text{SO}_2 \text{NHR} \rightarrow \text{RHN</SO</HR>NH}_2 \quad \text{N=N} \quad \text{SO}_2 \text{NHR} \quad +2\text{H}^+ + 2e^-
\]

4,4'-disulphonamido(-R)hydroazobenzene

\[
\text{RHN</SO</HR>NH}_2 \quad \text{N=N} \quad \text{SO}_2 \text{NHR} \rightarrow \text{RHN</SO</HR>NH}_2 \quad \text{N=N} \quad \text{SO}_2 \text{NHR} \quad +2\text{H}^+ + 2e^-
\]

4,4'-disulphonamido(-R) azobenzene
To confirm it further, some of the sulpha drugs, namely, sulphadiazine, sulphaquanidine and sulphamethazine, were subjected to electrolysis using graphite electrodes of larger dimensions. After sometime, reddish brown layers of sizable thickness were seen to be formed around each graphite electrode. These coloured compounds on analysis were found to be 4,4’-disulphonamido (-R) azobenzene. It is thus clear that the anodic oxidation of sulpha drugs involves two electron change.

**Estimation of sulpha drugs in pharmaceutical preparation**

Linear sweep voltammetry, at the tubular graphite electrode, has been used for the estimation of sulpha drugs present in some commonly available pharmaceutical preparations. For this purpose solutions of different concentrations varying between $10^{-5}$ to $10^{-4}$ M are prepared for each of the sulpha drug in 0.1 M H$_2$SO$_4$. The current potential curves for each of the concentration are recorded, keeping the velocity of the solution constant and the peak currents are calculated. In this way, the current concentration data are obtained for each of the sulpha drug. These data are then plotted in the current concentration graphs. In all cases the graphs are linear.

Under similar conditions, current-potential curves for solution samples of some easily available pharmaceutical preparations containing different sulpha drugs derivatives,
in 0.1 M $\text{H}_2\text{SO}_4$, are recorded and concentration corresponding to each peak current is calculated from current-concentration graph. The data obtained are given in Table VII. As can be seen the amount of sulpha drug per tablet determined voltammetrically comes out to be quite close the reported value. Thus linear sweep voltammetric technique for carrying out the estimation of sulpha drugs is highly dependable.
Table VII: Estimation of sulpha drugs in pharmaceutical preparations

<table>
<thead>
<tr>
<th>Pharmaceutical preparation</th>
<th>Compound present</th>
<th>Amount present per table (mg)</th>
<th>Amount determined per table (mg) voltametrically</th>
<th>Amount reported by Bansal (192)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Sulfadiazine (May and Baker)</td>
<td>Sulfadiazine</td>
<td>500</td>
<td>498.20</td>
<td>497.00</td>
</tr>
<tr>
<td>2. Adiazine (Dolpham)</td>
<td>Sulfadiazine</td>
<td>500</td>
<td>496.00</td>
<td>499.00</td>
</tr>
<tr>
<td>3. Sulfaguanidine (May and Baker)</td>
<td>Sulfaguanidine</td>
<td>500</td>
<td>501.20</td>
<td>495.00</td>
</tr>
<tr>
<td>4. Sulfathiazole (May and Baker)</td>
<td>Sulfathiazole</td>
<td>500</td>
<td>498.50</td>
<td>498.00</td>
</tr>
<tr>
<td>5. Cilcosin (Ciba)</td>
<td>Sulfasomidine</td>
<td>500</td>
<td>502.80</td>
<td>500.00</td>
</tr>
</tbody>
</table>

Electrode length = 1.0 cm  
Velocity = 1.0161 cm sec^{-1}  
Scan rate = 1.0 V min^{-1}