Indian Journal of Chemistry
Vol. 27A, September 1988, pp. 825-826

Differential Pulse Polarographic Determination of Proquazone

AYTEKIN TEMIZER*, SEDEF KIR & A NUR ONAR
Department of Analytical Chemistry, Faculty of Pharmacy, Hacettepe University, 06100, Ankara, Turkey

Received 3 *September* 1987; *revised and accepted* 28 *January* 1988

The differential pulse polarographic (DPP) behaviour of proquazone is investigated in different media. The compositions of electrolytes, height of the mercury column, temperature and the other parameters are so selected that the determination of this substance can be accomplished down to sub ppm level. Evidence is presented to show that the reduction of proquazone to proquazole is a reversible reaction with one electron transfer.

Proquazone [1-isopropyl-4-phenyl-7-methyl-2-(1H)-quinazolinone] is a new non-steroidal, anti-inflammatory agent. The compound possesses potent anti-inflammatory, analgesic and antipyretic effects[1].

Earlier, proquazone has been determined in serum and in synovial fluid by means of fluorimetric procedures with detection limit of 0.01 μg/ml[2,3]. The concentrations of the principal metabolite were determined by means of HPLC with the detection limit lying in the range 0.03-0.05 μg/ml[3]. However, the earlier methods of determination are cumbersome. We present here a differential pulse polarographic method of the determination of proquazone which can be used for the pure substance as well as for commercially available pharmaceutical samples.

The electrochemical apparatus used in the present study has been described previously[4]. The tapered dropping mercury electrode capillary that was used had a flow rate of 0.48 mg.s^{-1} at *p*H 5.00 (Britton-Robinson buffer) in open circuit with 80 cm height of mercury column. IR and UV spectrophotometers used were Perkin-Elmer model 457 and Beckman model DB-GT respectively. Controlled-potential electrolysis with a mercury pool cathode was carried out with the Heath model EUA-19-21 instrument. Corning model 12 research *p*H meter was used for *p*H measurements.

Stock solutions of $10^{-3}M$ proquazone were prepared in ethanol. The polarograms were recorded under the following conditions: drop-time, 1 s; modulation amplitude, 50 mV; current range, 2 μA; scan rate, 2 mV-s^{-1}; low pass filter, off; height of mercury column, 80 cm; temperature of the cell, 20 ± 0.1°C.

Controlled-potential electrolysis was performed using 18 ml of proquazone solution (90 μg/ml) in Britton-Robinson buffer at *p*H 5.00. Exhaustive reduction of proquazone at a mercury pool electrode was carried out. The potential of electrolysis was selected (with respect to SCE) so as to be similar to that on the upper plateau of the polarographic wave. At this potential, carbonyl group present on the molecule is reduced to hydroxyl.

In the determination of pharmaceutical samples, 5, 10 and 20 capsules were weighed. After finding the mean weight value of each set of capsules, the material from one capsule was dissolved in ethanol and solution diluted to 100 ml with the same solvent. 0.05 ml of this solution was added to the polarographic cell containing supporting electrolytes. Standard addition technique was used in order to find the concentration of drug.

The polarographic behaviour of proquazone was examined over the *p*H range 2-12. Proquazone gives rise to a single cathodic peak throughout the *p*H region studied. However, the peak potential becomes markedly more negative as the *p*H increases. The current value at peak potential (− 0.8 V) has been found to be highest in a supporting electrolyte composed of BR buffer of *p*H 5.00.

It is worth emphasizing that a buffer system at the usual concentrations used, generally provides adequate capacity only over ± 1 pK_a range. The pK_a of a polarographically active substance can be found by determining the inflection point of a plot of half-wave potential with respect to *p*H[5]. The inflection point for proquazone under the experimental conditions was found to be 4.40. Solutions having *p*H values near to this value seem to be appropriate as supporting electrolytes. In fact, BR buffer of *p*H 5.00 was found to be the best supporting electrolyte.

The characteristics of linear regression of calibration graph for proquazone at *p*H 5.00 BR buffer were: slope, 4.20×10^{-6} nA/*M*, concentration intercept, 0.53×10^{-6} *M* and correlation coefficient was 0.999 for 9 data points. The concentration range of 0.02-20 ppm is appropriate for the determination of proquazone by DPP. At concentrations lower than 0.02 ppm, the peak is not resolved from the noise. At concentrations greater than 20 ppm, deviation from linearity occurs.

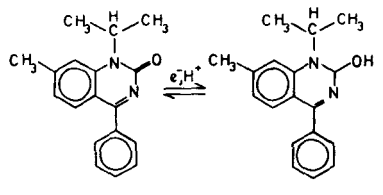

Fig. 1—Reduction mechanism of proquazone to proquazole

The mechanism of reduction of proquazone in aqueous solution involves the addition of one electron and a proton to form the corresponding proquazole (Fig. 1). This is shown by the controlled-potential electrolysis. The electrode product was isolated and identification was made by spectroscopic methods. An absorption peak at 360 nm belonging to the $\pi \rightarrow \pi^*$ transition of proquazone was not observed in the spectrum of proquazole. IR spectra of proquazone and proquazole are similar with the exception of a strong carbonyl stretching absorption at 1659 cm^{-1} in the spectrum of proquazone and a wide hydroxyl stretching vibration at 3400 cm^{-1} in the spectrum of proquazole.

In order to find the current characteristics, which were used in the analysis of proquazone, effect of the height of the mercury column and temperature coefficient have been determined. Linear regression analysis of the limiting current versus the square root of the height of the mercury column showed a linear behaviour. Temperature coefficient of the proquazone was found to be 1.5 %. deg^{-1}. These results indicate that the current is diffusion controlled.

The reversibility test was performed by scan reversal pulse polarography, logarithmic analysis and on the basis of the value of $E_{3/4}$-$E_{1/4}$. The reciprocal slope of the plot of logarithmic functions of current $(i_d\text{-}i)/i$ versus potential give the value 0.062 volt. This is very similar to the theoretical Nernst voltage of 0.059 volt, of 2.303 RT/nF for a reversible reduction involving one electron. The value of $E_{3/4}$-$E_{1/4}$ was found to be 59.375 mV. There was no difference found in reverse scanning. All these results showed that the electrode reaction is a reversible one.

Proquazone is marketed in a capsule form under the name "Biarison" containing 200 mg proquazone per capsule. Differential pulse polarographic analysis of Biarison capsules showed 196.37 ± 3.66 mg proquazone per capsule. Considerable time saving, increased reproducibility and precision were obtained with the use of DPP in determination of proquazone in Biarison capsules.

References

1 Andersen R B & Halskov O, *Scand J Rheumatology Suppl*, **21** (1978) 18.
2 Ross A & Hinderling P H, *J Pharm Sci.*, **70** (1981) 252.
3 Ott H & Meier J, *Scand J Rheumatology Suppl*, **21** (1978) 12.
4 Onar A N & Temizer A, *Analyst*, **112** (1987) 227.
5 Kucharczyk N, Adamovsky M, Horak V & Zuman P, *J electroanal Chem*, **10** (1969) 503.