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SPECTROPHOTOMETRIC DETERMINATION OF NOVALGIN IN TABLETS BY USE OF POTASSIUM IODATE

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Summary—An indirect colour reaction has been studied for determination of novalgin in tablets The method is simple, rapid and reproducible with a relative standard deviation of 0 2% Novalgin is determined spectrophotometrically by means of its colour reaction with potassium iodate Beer's law is obeyed over the range 1–10 mg of drug. A tentative reaction mechanism has been proposed

Novalgin (analgin, dipyrone) is the sodium salt of (2,3 - dihydro - 1,5 - dimethyl - 3 - oxo - 2 - phenyl - 1H-pyrazol-4-yl)ethylaminomethane sulphonic acid It is a commonly used analgesic Its determination in tablets is, therefore, very important. It has been determined in tablets and injections by high-performance liquid chromatography on a reversed-phase column, with ultraviolet detection.[1] Its spectrophotometric determination has been achieved by reaction with cerium(IV) and measurement of the resulting cerium(III) with arsenazo III [2] Antipyrine and pyramidone can also be determined by this method. A coulometric method for novalgin determination in tablets has also been reported.[3] It has also been determined spectrophotometrically by reaction with *N*-bromosuccinimide in acid media and measurement of the absorbance of the product at 290–450 nm.[4] Antipyrine and amidopyrine also give a positive reaction. A number of spectrophotometric methods for novalgin and other analgesics have been reported based on use of potassium ferrocyanide,[5] sodium nitrite,[6] 4-dimethylaminobenzaldehyde,[7] Bromophenol Blue[8] and potassium aurichloride[9] as reagents In our studies, novalgin has been found to interact with potassium iodate in presence of hydrochloric acid, to produce a yellowish red solution This colour reaction has been studied for spectrophotometric determination of the drug.

EXPERIMENTAL

Apparatus

A Bausch and Lomb Spectronic-20 was used for absorbance measurement

Reagents

All chemicals used were of analytical grade

A 0 5% w/v novalgin solution was prepared in distilled ethanol The tablets used were purchased locally A 0 1*M* potassium iodate solution and 1.0*M* hydrochloric acid were prepared with conductivity water

Procedure

To an aliquot of novalgin solution (containing 1–10 mg of the drug) in a 50-ml standard flask add 1 ml of 0.1*M* potassium iodate followed by 1 ml of 1*M* hydrochloric acid Let the reaction mixture stand for about 5 min for the yellowish red colour to develop, then dilute to the mark with water Measure the absorbance at 460 nm against a reagent blank

Procedure for analysis of formulations

Stir a known weight of finely ground tablets or capsule contents (equivalent to 25 mg of novalgin) with 30 ml of distilled ethanol for 10 min Filter off any residual solid on a Whatman No 42 paper Make up the filtrate to volume in a 50-ml standard flask, then apply the procedure above

RESULTS

A number of organic compounds were tested and it was found that novalgin gives a characteristic yellowish red colour Many other drugs and a wide range of other compounds containing different groups were found to give a negative test Those tested included the following

Drugs etc Aspirin, codeine sulphate, oxyphenbutazone, propyphenazone, phenylbutazone, phenazone salicylate, phenacetin, caffeine, diazepam nicotine and nicotinamide could be tolerated in amounts up to 1 mg in determination of 2 mg of novalgin

Amino-acids Histidine, aspartic acid, glutamic acid, leucine, lysine, glycine, tryptophan, asparagine, arginine, L-alanine, β-alanine and tyrosine.

Acids Acetic, formic, oxalic, citric, malic, adipic, propionic, tartaric and pyruvic

Sugars Glucose, fructose, rhamnose, sucrose, maltose, arabinose and xylose

Aldehydes Acetaldehyde, benzaldehyde, crotonaldehyde and anisaldehyde.

Ketones. Acetone, ethyl methyl ketone, diethyl ketone, methyl propyl ketone and cyclopentanone

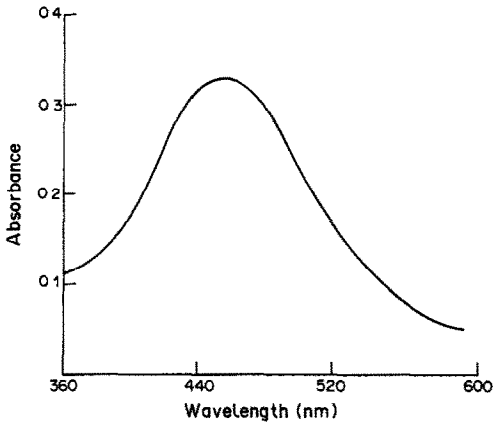


Fig 1 Absorption spectrum of reaction product

Amines. Ethyl, methyl, butyl, propyl, diethyl and triethyl

Alcohols. Ethanol, methanol, propanol and butanol

Other compounds Acetanilide and vitamin B complex.

Absorption spectrum

The absorption spectrum of the reaction product is shown in Fig 1 The optimum wavelength is 460 nm

Optimum conditions

The absorbance of the product was found to be constant for up to 30 min and then slightly decreased

With 5 0 mg of novalgin, absorbances of 0 05, 0.14, 0.28, 0.31, 0 33, 0 33, 0 33 and 0 33 were obtained

Table 1 Determination of novalgin (analgin) in pharmaceutical preparations (average and coefficient of variation, 5 replicates)

Drug and supplier	Nominal composition, *mg*	Found by* present method, *mg*	C V %	Found by comparison method, *mg*	Reference for comparison method
1 Baralgan (Hoechst)	500 analgin 5 *p*-piperidinoethoxy-*O*-carbmethoxy benzophenone hydrochloride 0 1 diphenylpiperidinoethyl acetamide–brom-*O*-methylate	505	0 3	509	18
2 Maxigesic (ETHICO)	250 analgin 100 oxyphenbutazone 2 5 diazepam	244	0 6	—	—
3 Spasmizol (IDPL)	500 analgin 2 5 homatropine methyl bromide 10 phenobarbitone	504	0 1	498	18
4 Ginox (Averest Chem Lab)	500 analgin 100 oxyphenbutazone	510	0 3	515	18
5 Promalgin (Uniloids)	250 analgin 250 paracetamol 25 caffeine	264	0 5	—	—
6 Maxigon (Unichem)	500 analgin 5 *p*-piperidinoethoxy-*O*-carbmethoxy benzophenone hydrochloride	495	0 4	499	18
7 Algesin-O (Alembic)	300 analgin 100 oxyphenbutazone	293	0 7	298	18
8 Spasmolysin (Std Pharm)	500 analgin 10 dicyclomine hydrochloride	514	0 1	520	18
9 Pamagin (Alkem)	500 analgin 5 diazepam	459	0 5	—	—
10 Ultragin (Manner)	250 analgin 250 paracetamol 25 caffeine	256	0 6	257	18
11 Zamalgin-A (Rallis)	250 analgin 15 caffeine 5 codeine phosphate	255	0 8	258	17
12 Largesic (Lark Lab)	500 analgin 100 oxyphenbutazone 100 magnesium trisilicate	474	0 2	—	—
13 Sedyn-A Forte (M M Labs)	375 analgin 2 5 diazepam 20 diphenhydramine hydrochloride	324	0 7	—	—
14 Neogene (AFD)	200 analgin 250 paracetamol 7 5 chlorpromazine hydrochloride	250	0 2	253	18
15 Anadex (Concept)	250 analgin 65 dextropropoxyphenhydrochloride	249	0 2	259	17
16 Oxalgin (Cadila)	500 analgin 100 oxyphenbutazone	535	0 4	531	17

with 0 32, 0.34, 0.36, 0.40, 0 48, 0 50, 0.60 and 0.70 ml of 0.1*M* potassium iodate. It is clear from these data that 5.0 mg of novalgin needs at least 0.48 ml of 0 1*M* potassium iodate for reaction to be complete. However, the use of a larger volume does not affect the absorbance Therefore, 1 ml of 0.1*M* potassium iodate is recommended for the determination of novalgin. It was similarly found that 1 ml of 1*M* hydrochloric acid is the optimum volume.

Conformity with Beer's law

Beer's law holds good over the range 1–10 mg of novalgin The molar absorptivity is $0\,1 \times 10^4$ l mole^{-1} cm^{-1} The correlation coefficient for calibration was 0.99

Ten replicate determinations of 2.0 mg of novalgin gave a standard deviation of 3 μg (relative standard deviation 0.2%)

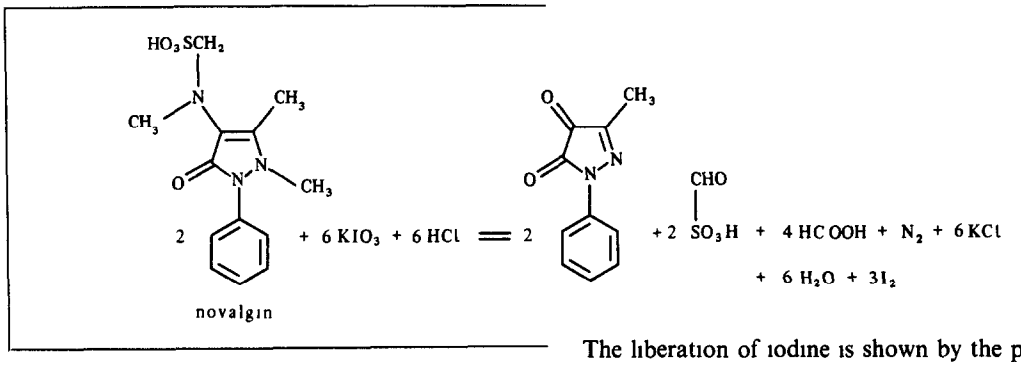
The interference tests are described above.

Applications

The method was used to determine novalgin in various pharmaceutical preparations. The results are shown in Table 1. None of the other ingredients of the samples reacts with either iodine or iodate

DISCUSSION

The methods for the determination of various organic compounds by oxidation with potassium iodate have been discussed in greater detail elsewhere [10] The iodine liberated during the course of reaction is distilled off and determined. The oxidation reaction in acidic medium depends on both the substrate and the experimental conditions. Reaction is favoured by the presence of hydrogen atoms bound to carbon atoms activated by a functional group.[11–14] In particular, hydrogen atoms on aromatic nuclei with electron-donating substituents are very reactive towards iodate The reaction occurs in acidic media and the rate depends on the concentration of iodate Cavazutti *et al.*[15] examined the reactivity of iodic acid with many classes of compounds of pharmaceutical interest, in order to establish its potential for detecting and identifying drugs separated by thin-layer chromatography on silica gel layers, since potassium iodate had already been used successfully for staining sympathomimetic amines [16] On the basis of these studies, a tentative reaction mechanism is proposed Potassium iodate interacts with the drug in presence of hydrochloric acid to liberate iodine



novalgin

The liberation of iodine is shown by the production of a blue colour with starch

REFERENCES

1 N H Eddine, F Bressolle, B Mandrou and H Fabre, *Analyst*, 1982, **107**, 67
2 F Buhl and U Hachula, *Chem Anal Warsaw*, 1981, **26**, 395
3 N Kosta, V Ksenija and M Mirjana, *Acta Pharm Jugosl*, 1984, **34**, 177
4 N V Pathak and I C Shukla, *J Indian Chem Soc*, 1983, **60**, 206
5 P George, *Indian J Pharm*, 1974, **36**, 14
6 H Abdine, A S Sophi and G I Morcas Magdi, *Pharm Sci*, 1973, **62**, 1834
7 R Bontemps, J Parmentier and M Diesse, *J Pharm*, 1968, **23**, 222
8 D M Shinghal, *Indian Drugs Pharm Ind*, 1976, **11**, 37
9 N Shiritsu and D Yakugakuku, *Kenbyu Nomo*, 1965, **13**, 1
10 W Hurka, *Mikrochemie*, 1944, **31**, 83
11 R J Williams, E Rohrman and B. E Christensen, *J. Am Chem. Soc*, 1937, **59**, 281
12 J O Edwards, *Chem Rev*, 1952, **50**, 461
13 R A Garrett, R J Gillespie and J B Senior, *Inorg Chem*, 1965, **4**, 563
14 K Nabesima, *Okayama Igakki Zasshi*, 1939, **51**, 1331
15 G Cavazzutti, L Gagliavdi, A Amato, M Profili and V J Zagarese, *J Chromatog*, 1983, **263**, 528
16 K Macek and I M Hais, in *Handbuch der Papierchromatographie*, G Fisher (ed), Band I, Verlag-Jena, Jena, 1958
17 *Pharmacopoeia of India*, Vol I, p 44, 1985
18 L Viktor, *Acta Pharm Hung*, 1971, **41**, 51