3. Analytical procedure for method B

Aliquots of standard RXF solution (0.2–1 ml) were taken in a series of 10 ml volumetric flask and 1 ml of 0.5% ferric chloride solution was added follow by potassium ferric cyanide, thoroughly mixed and absorbance measured at 430 nm against blank solution. A calibration curve has drawn by plotting absorbance reading against drug concentration. The amount of the drug was calculated from the standard calibration graph.

4. Analytical procedure for the the formulation

A tablet powder equivalent to 100 mg RXF was weighed accurately and transferred to a 100 ml volumetric flask. The content was dissolved in methanol and made up to the volume with methanol. The procedure mentioned in method A and method B is repeated.

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Determination of peroxide values using ethyl acetate as solvent

Analytical methods in respect to environmental and economical concern, part 21*

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Peroxide values of fixed oils can be determined in ethyl acetate, an easily biodegredable solvent instead of chloroform according to PH. EUR. 2002, method A. Potentiometric indication is recommended. Further investigations are necessary to explain the high blank values obtained, when ethyl acetate is used.

The peroxide value is the number that expresses the quantity of peroxide in 1000 g of the substance in milliequivalents of active oxygen. The peroxide-number is an important indication of the degree of rancidity of fats (Bracher 2002). PHARM. EUR. 2002 determines the peroxide value according to two methods. Method A uses chloroform as solvent and is applied in most of the monographs. In order to avoid the use of environment hazardous chlorinated hydrocarbons, method B employs 2,2,4-trimethylpentane (isooctane). But the latter method is not without problems. Since trimethylpentane floats on the aqueous layer, the transition of the iodine from the organic phase into the aqueous medium is delayed very much. PH. EUR. recommends to add a small amount of a high HLB nonionogenic emulsifier for example polysorbate 60. A validation is necessary, if method B is used instead of method A.

Ethyl acetate can replace chloroform in the determination of the iodine value of fixed oils (Hilp 2004a). But starch solutions do not yield the characteristic blue colour with iodine in the presence of ethyl acetate. Above all, with application of 0.01 M $Na_2S_2O_3$ the change of the indicator is difficult to recognise. Nevertheless, if potentiometric titration is used, a definite potential jump (Hilp, 2002b, 2004a) can be observed. Furthermore, ethyl acetate shows a fine distribution in water, when stirred. A fast transition of iodine in the aqueous phase can be recognised.

The Table shows the determination of peroxide values of three fixed oils. On purpose, old arachis oils and sesame oil, whose expiration date was exceeded, were used to get a high peroxide value. PH. EUR. 2002 demands for castor oil a peroxide value not over 10.0, because only recently pressed oil yields a value below 5.0 (Arens and Brühl 2002).

When using ethyl acetate as solvent high blank values are conspicuous. Above all, the registration of the poten-

Table: Determination of peroxide values of fixed oils using ethyl acetate as solvent in comparison to PH. EUR. 2002, Method A

Material Demanded peroxide value	Weight of sample (g)	Determination (Ethyl acetate as solvent)										PH. EUR. 2002, Method A			
		Visual					Potentiometric					Visual			
		n	Blank value	Mean	Bias[a] (%)	RSD (%)	n	Blank value	Mean	Bias[a]	RSD (%)	n	Blank value	Mean	RSD (%)
Arachis oil[b], peanut oil ≤ 5.00	5.000 – 5.071	7	0.659	29.7	−10.0	0.79	7	0.724	30.0	−9.7	1.17	7	0.000	32.9	0.51
Castor oil ≤ 10.00	5.010 – 5.375	7	0.525	3.50	−12.7	4.10	7	0632	3.76	−6.6	4.62	7	0.000	4.01	1.49
Sesame oil[b] ≤ 5.00	5.005 – 5.104	7	0.612	7.26	−0.10	4.00	7	0.808	7.21	−0.75	4.92	7	0.000	7.26	2.29

[a] in comparison to PH. EUR. 2002, method A
[b] Expiration date was 4 years exceeded

tiometric indication is improved with low peroxide values, when the blind-values are high. The reason could not be declared. Perhaps, this may be caused by stabilisers of the solvent or components from the polyethylene bottles. No blind-values were found when using chloroform.

With ethyl acetate as solvent significant lower values were found than according to the method A of PH. EUR. 2002. Also the precision of method A of PH. EUR. 2002 is better.

On the other hand, for method B the percentage relative standard deviation (coefficient of variation) concerning the repeatability is reported between 4.1 and 11.5 and concerning the reproducibility between 10.7 and 38.3 for peroxide values between 1.3 and 24.1 for fixed oils and fats (ISO 3960 : 2001). These ISO instructions demand for peroxide-values ≤ 10, that the absolute difference between two independent single test results shall not be larger than 10% of the mean of the two results in more than 5% of cases concerning the repeatability resp. 75% concerning the reproducibility. Furthermore a comparison of peroxide values is allowed only on the basis of the same method for determination (DFG – Einheitsmethoden 2002)

Therefore, the method with ethyl acetate should be employable. However, further investigations are necessary.

Experimental

1. Instrumentation, materials, and solution

see Hilp (2000a, 2000b) ethyl acetate, [141–78-6], extra pure, Merck art. 100864, 0.01 M $Na_2S_2O_3$ was prepared by dilution of 0.1 M solution and standardized with 20,0 ml of 0.001667 M KIO_3, 10 ml of 0.25 M NaAc – 10 M HAc, 5 ml of 0.2 M KI and potentiometric indication.

2. Determination of peroxide values using ethyl acetate as solvent

About 5.00 g of the sample, accurately weighed, are dissolved in 20 ml of ethyl acetate and 20 ml of glacial acetic acid using a 250 ml iodine flask. 0.5 ml of a saturated solution of potassium iodide is added and shaken for exactly 1 min. After immediate addition of 25 ml of H_2O the titration is performed with 0.01 M $Na_2S_2O_3$ and visual or potentiometric indication. A blind value has to be determined under the same conditions. The calculation takes place according to method A of PH. EUR. 2002

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* Part 20 (Hilp 2004b)

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