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A Comparative Study of the Hydroxyl Value and Iodine Value in Polyoxyl Stearyl Ether in United States Pharmacopeia Specifications

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Abstract

The iodine value (iodine number) and hydroxyl value are important analytical characteristics of fats and oils. The iodine (I_2) required saturating the fatty acids present in 100 grams of the oil or fat. Iodine value is a measure of the total number of double bonds (-C=C-) present in fats and oils. Unsaturated compounds contain molecules with double and triple bonds which are very reactive towards iodine. The iodine value has been determined according to Hanus with iodine monobromide in glacial acetic acid, and then the amount of iodine remaining unreacted is determined by titration using sodium thiosulfate volumetric standard solution. The hydroxyl value is the amount of potassium hydroxide in milligrams that is equivalent to the hydroxyl amount of 1 gram of the sample (mg KOH/g sample). Poloxyl Stearyl Ether is a mixture of the monostearyl ethers of mixed polyethylene glycols. It may contain various amounts of free stearyl alcohol and some free polyethylene glycol. In this study, the iodine value and hydroxyl value have been determined by titration in polyoxyl stearyl ether. Iodine value 1.84 g of I_2 absorbed/100g sample, and hydroxyl value 162.65 mg KOH/g sample have been found in poloxyl stearyl ether. The iodine value and hydroxyl value results met the United States Pharmacopeia specifications for Polyoxyl Stearyl Ether.

Keywords

Iodine Value, Hydroxyl Value, Hanus Method, Polyoxyl Stearyl Ether

1. Introduction

The fatty acids, used to prepare surfactants, may contain saturated or unsaturated alkyl chains. Since unsaturated chains pack differently in crystalline and polymorphic forms, substantial differences in functionality may be observed

with variation in unsaturated content. Unsaturated chains are also vulnerable to oxidative degradation [1].

Main surfactants are used in the pharmaceutical field. In the pharmaceutical field surfactants are used especially as emulsifiers, solubilizers, and wetting agents [2]. In pharmaceutics, the term *cream* is traditionally used to describe semisolids with a relatively fluid viscosity that are formulated as oil-in-water emulsions and that are aesthetically favorable and easy to spread. Creams may be capable of penetrating the different layers of the skin, particularly the horny layers [3].

Reagents, which add across carbon-carbon double bonds, have been used to determine the degree of unsaturation since the early years of organic chemistry. Two commonly accepted methods for determination of Iodine Value have been developed: 1) Wijs' Method, reacts iodine monochloride with surfactant in carbon tetrachloride. Excess reagent is then titrated with standard thiosulfate solution. 2) The Hanus Method is nearly identical but employs iodine monobromide as the reagent. Because of the high toxicity of carbon tetrachloride, a modified method has been developed which uses cyclohexane as the solvent [1].

Poly Stearyl Ether (Steareth), Non-ionic surfactant, Polyether, Alcohol Polyether, Alcohol Polyoxyethylene Ether, Linear Alkanol Polyoxyethylene Ether. *Systematic name*: Octadecan-1-ol, ethoxylated, Surface active agents—Detergents. *Synonyms*: Polyoxyethylated stearyl alcohol, Stearyl alcohol, ethoxylated, Stearyl alcohol ethylene oxide, Polyethylene glycol monostearyl ether.

The molecular formula is (C_2H_4O) $n.C_{18}H_{38}O$, Molecular Weight is 313.542, structure is in **Figure 1**. Poly Stearyl Ether is stable, white flake or granular, dispersible in water to soluble in water. The solubility increases with the increase of EO number. Solid form: flammable material; irritation, irritation to skin, eye, respiratory system. Harmful products of combustion are CO, CO_2 and so on. Contact with strong oxidants can cause burns. May be hazardous to environment, water body should be given special attention. Poly Stearyl Ether excellent cleansing, emulsifying, dispersing, solubilizing, wetting, and permeating abilities. Performance is related to EO number [4].

Polyoxy Stearyl Ether is a mixture of the monostearyl ethers of mixed polyethylene glycols, and average polymer length is equivalent to not less than (NLT) 2 and not more than (NMT) 20 oxyethylene units (nominal value). It may contain various amounts of free stearyl alcohol and some free polyethylene

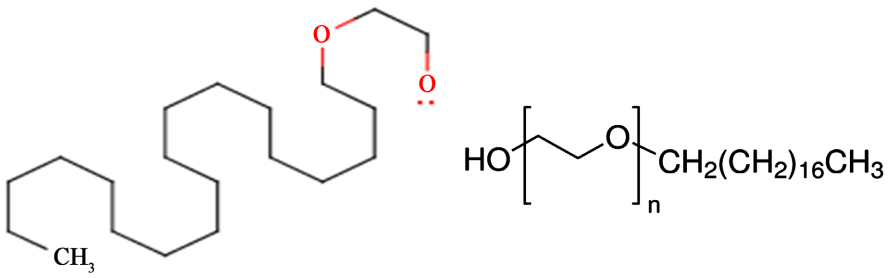

Figure 1. Molecular Structure of poly Stearyl Ether (Me: methyl group, CH_3).

glycol [5]. Poly Stearyl Ether is a permeation enhancer, used as a surfactant; used to make cosmetics, cleaning-maintenance-laundry products, construction chemicals, coatings, inks, metalworking fluid concentrates, lubricants-greases, textile dying-finishing-impregnating products, metal surface treatment products (including those for galvanizing and electroplating), in polymerization reactions, plant protection-seed treatment products, textile and leather manufacture, and as a laboratory reagent; Permitted for use as an inert ingredient in non-food pesticide products; [EPA]. Poly Stearyl Ether has pH of aqueous solution is 5.0 - 7.0 [4].

Impurities:

Information was not available as to the possible presence of a trace amounts of 1,4-dioxane or other impurities in the Polyoxyethelene Stearyl Ether (steareth) compounds [6].

2. Materials and Method

2.1. Determination of Hydroxyl Value

In analytical chemistry, the hydroxyl value is defined as the number of milligrams of potassium hydroxide (KOH) required to neutralize the acetic acid taken up on acetylation of one gram of a chemical substance that contains free hydroxyl groups. The analytical method used to determine hydroxyl value traditionally involves acetylation of the free hydroxyl groups of the substance with acetic anhydride in pyridine solvent. After completion of the reaction, water is added, and the remaining unreacted acetic anhydride is converted to acetic acid and measured by titration with potassium hydroxide.

The hydroxyl value can be calculated using the following equation. Note that a chemical substance may also have a measurable acid value affecting the measured endpoint of the titration. The acid value (AV) of the substance, determined in a separate experiment, enters into this equation as a correction factor in the calculation of the hydroxyl value (HV):

$$(56.11\ N/W)[B + (WA/C) - T]$$

The content of free hydroxyl groups in a substance can also be determined by methods other than acetylation [7]. Determinations of hydroxyl content by other methods may instead be expressed as a weight percentage (wt. %) of hydroxyl groups in units of the mass of hydroxide functional groups in grams per 100 grams of substance. The conversion between hydroxyl value and other hydroxyl content measurements is obtained by multiplying the hydroxyl value by the factor 17/560 [8]. The chemical substance may be a fat, oil, natural or synthetic ester, or other polyol [9].

ASTM D 1957 [10] and ASTM E222-10 [11] describe several versions of this method of determining hydroxyl value.

2.1.1. Apparatus

- Burette.
- Pipette.

- Magnetic starrier, thermally insulated.
- Fluoropolymer coated magnetic bar.

2.1.2. Reagents and Solutions

- Polyoxyl stearyl ether [CAS No. 9005-00].
- Pyridine-Acetic Anhydride Reagent (3:1).
- 0.5 N alcoholic potassium hydroxide TS.
- Butyl alcohol.
- Phenolphthalein TS-Dissolve 1 g of phenolphthalein in 100 mL of alcohol.

2.1.3. Method

The Hydroxyl Value is the number of mg of potassium hydroxide equivalent to the hydroxyl content of 1.0 g of the substance (see Table 1).

Pyridine-Acetic Anhydride Reagent—Just before use, mix 3 volumes of freshly opened or freshly distilled pyridine with 1 volume of freshly opened or freshly distilled acetic anhydride.

Procedure—Transfer a quantity of the substance (see Table 2), determined by reference to the accompanying table and accurately weighed, to a glass-stoppered, 250-mL conical flask, and add 5.0 mL of Pyridine-Acetic Anhydride Reagent. Transfer 5.0 mL of Pyridine-Acetic Anhydride Reagent to a second glass-stoppered, 250-mL conical flask to provide the reagent blank. Fit both flasks with suitable glass-jointed reflux condensers, heat on a steam bath for 1 hour, add 10 mL of water through each condenser, and heat on the steam bath for 10 minutes more. Cool, and to each add 25 mL of butyl alcohol, previously neutralized to phenolphthalein TS with 0.5 N alcoholic potassium hydroxide, by pouring 15 mL through each condenser and, after removing the condensers,

Table 1. Specification: within the ranges specified in the table.

Oxyethylene Units/Molecule (Nominal Value)	Hydroxyl Value
2	150 - 180
10	75 - 90

Table 2. Mass of test portion for hydroxyl value.

Hydroxyl Value Range	Weight of Test Specimen (g)
0 - 20	10
20 - 50	5
50 - 100	3
100 - 150	2
150 - 200	1.5
200 - 250	1.25
250 - 300	1
300 - 350	0.75

washing the sides of both flasks with the remaining 10-mL portions. To each flask add 1 mL of phenolphthalein TS, and titrate with 0.5 N alcoholic potassium hydroxide VS, recording the volume, in mL, consumed by the residual acid in the test solution as T and that consumed by the blank as B. In a 125-mL conical flask, mix about 10 g of the substance, accurately weighed, with 10 mL of freshly distilled pyridine, previously neutralized to phenolphthalein TS, add 1 mL of phenolphthalein TS, and titrate with 0.5 N alcoholic potassium hydroxide VS, recording the volume, in mL, consumed by the free acid in the test specimen as A. Calculate the Hydroxyl Value by the formula:

$$(56.11N/W)\left[B+(WA/C)-T\right]$$

in which W and C are the weights, in g, of the substances taken for the acetylation and for the free acid determination, respectively; N is the exact normality of the alcoholic potassium hydroxide; and 56.11 is the molecular weight of potassium hydroxide. If the Acid Value for the test substance is known, calculate the Hydroxyl Value by the formula:

$$(56.11N/W)\left[B-T\right]+\text{Acid Value}$$

in which W is the weight, in g, of the substance taken for the acetylation; N is the exact normality of the alcoholic potassium hydroxide; and 56.11 is the molecular weight of potassium hydroxide [12] [13].

Calculation of Hydroxyl Value

$$\text{Hydroxyl Value}=(56.11N/W)\left[B+(WA/C)-T\right]$$

$$\text{H.V}=\frac{48.18+\frac{2.00\times 0.55}{5.03}-37.54}{2.01}\times 0.539\times 56.11=161.72 \quad \text{mg KOH/g sample}$$

$$\text{Duplicate Hydroxyl Value}=\frac{48.18+\frac{2.00\times 0.55}{5.03}-37.47}{2.00}\times 0.539\times 56.11$$

$$=163.58\text{mg KOH / g sample}$$

Average result: 162.65 mg KOH/gram sample

% RPD= 1.14%.

2.2. Acid Value, (Free Fatty Acids) Method I <401>

The acidity of fats and fixed oils in this Pharmacopeia may be expressed as the number of mL of 0.1 N alkali required to neutralize the free acids in 10.0 g of substance. Acidity is frequently expressed as the Acid Value, which is the number of mg of potassium hydroxide required to neutralize the free acids in 1.0 g of the substance. Unless otherwise directed in the individual monograph, use Method I.

Method I

Procedure—Unless otherwise directed, dissolve about 10.0 g of the substance, accurately weighed, in 50 mL of a mixture of equal volumes of alcohol and ether (which has been neutralized to phenolphthalein with 0.1 N potassium hydroxide

or 0.1 N sodium hydroxide, unless otherwise specified) contained in a flask. If the test specimen does not dissolve in the cold solvent, connect the flask with a suitable condenser and warm slowly, with frequent shaking, until the specimen dissolves. Add 1 mL of phenolphthalein TS and titrate with 0.1 N potassium hydroxide VS or 0.1 N sodium hydroxide VS until the solution remains faintly pink after shaking for 30 seconds. Calculate either the Acid Value or the volume of 0.1 N alkali required to neutralize 10.0 g of specimen (free fatty acids), whichever is appropriate. Calculate the Acid Value by the formula:

$$56.11V \times N/W$$

in which 56.11 is the molecular weight of potassium hydroxide; V is the volume, in mL; N is the normality of the potassium hydroxide solution or the sodium hydroxide solution; and W is the weight, in g, of the sample taken. If the volume of 0.1 N potassium hydroxide VS or 0.1 N. sodium hydroxide VS required for the titration is less than 2 mL, a more dilute titrant may be used, or the sample size may be adjusted accordingly. The results may be expressed in terms of the volume of titrant used or in terms of the equivalent volume of 0.1 N potassium hydroxide.

If the oil has been saturated with carbon dioxide for the purpose of preservation, gently reflux the alcohol-ether solution for 10 minutes before titration. The oil may be freed from carbon dioxide also by exposing it in a shallow dish in a vacuum desiccator for 24 hours before weighing the test specimens.

2.2.1. Reagents and Solutions

- Alcohol.
- Eter.
- Phenolphthalein TS.
- 0.1 N Sodium Hydroxide VS.
- 0.1 N potassium Hydroxide VS.
- Analytical balance.

2.2.2. Calculations of Acid Value

$$\text{Acid Value} = \frac{56.11 \times 0.28 \times 0.1109 \text{ N KOH}}{5.023} = 0.347 \text{ mg KOH/g sample.}$$

$$\text{Acid Value} = \frac{56.11 \times 0.28 \times 0.1109 \text{ N KOH}}{5.014} = 0.347 \text{ mg KOH/g sample.}$$

2.3. Determination of Iodine Value (Number)

2.3.1. Apparatus

- Iodine flask.
- Burette.
- Pipette.
- Mechanical or Magnetic stirrer.
- Glass stoppered, wide mouth bottles or Erlenmeyer flask (500 mL).
- Stir bar.

All glassware used must be clean and dry [14].

2.3.2. Reagents

- Polyoxyl stearyl ether, Obtained from ChemIDplus. Chemical Numbering System CASRN: 9005-00-9.
- Iodobromide TS.
- Potassium iodide, KI: Sigma-Aldrich ACS reagent, ≥99%, CAS Number 7681-11-0.
- D. I. Water: Recently boiled and distilled or deionized water.
- 0.1 N sodium thiosulfate VS.
- Chloroform, HPLC Trade Grade, Sigma-Aldrich. CAS Number: 67-66-3. [Caution: Chloroform is a known carcinogenic and highly toxic. Do not breathe in vapor. Handle with extreme care. Wear safety glasses, and gloves. Use in well ventilated area all the time].

2.3.3. Solutions

- Potassium Iodide Solution: Dissolve 10.0 g anhydrous KI in 100 mL of water.
- Sodium Thiosulfate 0.1 N volumetric solution (VS), prepared by dissolving 24.9 g of sodium thiosulfate in distilled water and diluting to 1 L. Accurately standardized VS potassium dichromate primary standard as follows normal standardization procedures.

Standardization of $Na_2S_2O_3$

Pipet 20.0 mL of KIO_3 solution into a 125 mL Erlenmeyer flask and stir in about 1 g KI. Add 20 mL DI water. Add about 1 mL H_2SO_4. Immediately titrate the dark brown solution with $Na_2S_2O_3$ to a straw yellow color. Add 2 pipets full (about 4 mL) of starch solution. Continue the titration until the purple color just disappears and the solution becomes colorless. Calculate the $Na_2S_2O_3$ concentration using the titration equations.

$$IO_3^- + 5I^- \rightarrow 3I_2$$

and

$$3I_2 + 6S_2O_3^{2-} \rightarrow 6I^- + 3S_4O_6^{2-} \quad (i.e.\ 6\ \text{mmol}\ \ S_2O_3^{2-}\ \ \text{per mmol}\ \ IO_3^-).$$

Perform a duplicate and take the average [14].

858.0 mg KIO_3	20 mL KIO_3	mmol KIO_3	6 mmol S_2O_3	
	100 mL	214,001 mg	mmol KIO_3	43.4 mL S_2O_3

N = 0.11085 N.

856.0 mg KIO_3	20 mL KIO_3	mmol KIO_3	6 mmol S_2O_3	
	100 mL	214.001 mg	mmol KIO_3	43.3 mL S_2O_3

N = 0.11088 N; Ave. N = 0.1109 N.

- Starch Indicator Solution—Mix 1.0 g of soluble starch with sufficient cold water to make a thin paste. Add, while stirring, to 100 mL of boiling water. Mix and cool. Use only the clear solution [15].

2.3.4. Method

The Iodine Value represents the number of g of iodine absorbed, under the prescribed conditions, by 100 g of the substance. Unless otherwise specified in the individual monograph, determine the Iodine Value by Method I.

Method I (Hanus Method)

Procedure—Transfer an accurately weighed quantity of sample (see Table 3), as determined from the accompanying table, into a 250-mL iodine flask, dissolve it in 10 mL of chloroform, add 25.0 mL of iodobromide TS, insert the stopper in the vessel securely, and allow it to stand for 30 minutes protected from light, with occasional shaking. Then add, in the order named, 30 mL of potassium iodide TS and 100 mL of water and titrate the liberated iodine with 0.1 N sodium thiosulfate VS, shaking thoroughly after each addition of thiosulfate. When the iodine color becomes quite pale, add 3 mL of starch TS, and continue the titration with 0.1 N sodium thiosulfate VS until the blue color is discharged. Perform a blank test at the same time with the same quantities of the same reagents and in the same manner see Calculate the Iodine Value from the formula:

$$\text{Iodine Value} = \frac{\left[V_B - V_S\right] \times N \times 12.69}{W}$$

in which 126.90 is the atomic weight of iodine; V_B and V_S are the volumes, in mL, of 0.1 N sodium thiosulfate $Na_2S_3O_3$ VS consumed by the blank test and the actual test, respectively; N is the exact normality of the sodium thiosulfate $Na_2S_3O_3$ Volumetric Solution (VS); and W is the weight, in gram, of the substance taken for the test [Note—If more than half of the iodobromide TS is absorbed by the portion of the substance taken, repeat the determination, using a smaller portion of the substance under examination] [12] [13].

Calculation of Iodine Value

$$\text{Iodine Value} = \frac{(33.29 - 31.88) \times 0.1109 \times 12.69}{1.076} = 1.84 \text{ g } I_2/100 \text{ gram}$$

$$\text{Duplicate} = \frac{(33.29 - 31.90) \times 0.1109 \times 12.69}{1.070} = 1.83 \text{ g } I_2/100 \text{ gram}$$

Ave. Result = 1.84 g I_2/100 gram

%RSD = 2.18%.

Table 3. Mass of test portions for iodine value.

Iodine Value Expected	Weight in g ±0.1
<5	3
5 - 20	1
21 - 50	0.4
51 - 100	0.2
101 - 150	0.13
151 - 200	0.1

3. Results and Discussion

The test can be completed in a day, including cleaning the glassware at the end of the test.

For Blank determination, prepare a solution in the same way as indicated, but without a sample. Run one duplicate blank as well. It has been used monochloride iodide instead of iodobromide Test Solution (TS).

Waste material must be disposed of in accordance with the national and local regulations. The chemicals have been leave in original containers. No mixing with other waste [16].

Table 4. Results for acid value and hydroxyl value.

Sample weight (g)	Volume of Titrant (mL)	Acid Value mg KOH/g sample	Hydroxyl Value mg KOH/g sample
5.023	0.28	0.35	161.72
Dup. 5.014	0.28	0.35	163.58

Table 5. Results for acid value.

Weight of sample	Specification	Acid Value Results	Conforms (Y/N)
5.023	Not more than 1.0	0.313	Yes
Duplicate, 5.014	Not more than 1.0	0.313	Yes

Table 6. Specification and results of the analysis.

Identity	Specification	Result	%RSD	Confirm
Acid Value	Not more than 1.0 mg KOH/grams of the sample	0.32		Yes/Passes
Hydroxyl Value	148 - 165 (mg KOH/g of the sample)	162.7	1.14	Yes/Passes
Iodine Value	Not more than 2.0 g of I_2 absorbed/100g of the sample	1.84	2.18	Yes/Passes

4. Conclusion

We determined the hydroxyl and Iodine values of polyoxyl stearyl ether by United States Pharmacopeia. We observed that the values sample was within the range established at the USP specifications. The iodine number 1.84 g of I_2 absorbed/100 gram sample, and hydroxyl value 162.65 mg KOH/gram sample have been found in polyoxyl stearyl ether (see Tables 4-6). The results revealed that the USP-NF specification for polyoxyl stearyl ether.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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