

GOVERNMENT OF INDIA, THE PATENT OFFICE
214, ACHARYA JAGADISH BOSE ROAD
CALCUTTA-700017.

Complete Specification No. 16834/6 dated 7th December 1988.

Application and Provisional Specification No. 783/DEL/87 dated 7th September 1987.

Acceptance of the complete specification advertised on 16th March 1991

Index at acceptance— 32 F1 [IX (1)].

International Classification— C07D 307/91.

Title : IMPROVED PROCESS FOR THE MANUFACTURE OF
ERTHROSINE/EOSIN FROM FLUORESCHEIN.

Applicant : COUNCIL OF SCIENTIFIC AND INDUSTRIAL
RESEARCH, Rafi Marg, New Delhi-110001,
India, an Indian registered body incorporated
under the registration of Societies
Act (Act XXI of 1860).

Inventors : PAYYALLUR NARAYANAN ANANTHARAMAN &
MICHAEL NOEL.

The following specification describes the nature of this invention.

PRICE : TWO RUPEES

This invention relates to an improved process for the manufacture of erythrosine/eosin from fluorescein.

Hitherto it has been proposed to prepare Erythrosin/Eosin from fluorescein by iodination /bromination electrolytically using sodium carbonate or hydroxide containing a little excess iodine/sodium bromide or by chemical methods viz. i) the treatment of a comparatively cool alkaline solution of fluorescein and sodium iodide/sodium bromide with ammonium or potassium persulphate and ii) direct halogenation in hot acetic acid with excess of iodine/bromine.

These methods are open to the following objections: In the electrochemical method too much iodate/bromate is formed thereby reducing the current efficiency and yield. In the chemical method the purity of the compound is affected by the formation of dihalogen compounds instead of tetra halogen compounds thereby escalating the cost of production in the process of purification.

The object of this invention is to obviate these disadvantages by electrolytically halogenating fluorescein in sodium carbonate and boric acid or sodium bicarbonate in combination with iodine or sodium bromide at a stationary or rotating graphite or lead dioxide coated graphite electrode, using a current density ranging between 3.5 A/dm^2 at a temperature ranging between $30-40^\circ\text{C}$. Lead dioxide is deposited over a smooth graphite electrode. The electrolysis is carried out in a divided cell comprising of ceramic diaphragm and stainless steel cathode, anolyte being sodium carbonate and boric acid of 10% concentration each or sodium bicarbonate of 10% concentration containing fluorescein and iodine or sodium bromide and catholyte being sodium bicarbonate of 10% concentration. After passing the theoretical quantity of current (8 Faradays per mole of fluorescein) the solution is filtered to remove the suspended impurities and then neutralised with dilute sulphuric acid pH 2. The dye thus obtained is filtered, washed and dried in an air oven at a temperature less than 120°C .

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To these ends the invention broadly consists in halogenating a suspension of fluorescein in 10% sodium bicarbonate or 10% sodium carbonate with equivalent amount of boric acid with fluorescein upto 4% and equivalent quantity of iodine or sodium bromide and catholyte of 10% sodium carbonate or sodium bicarbonate respectively. A graphite or lead dioxide coated graphite acts as anode and stainless steel acts as cathode. The anode can be either stationary or rotating. A ceramic porous pot acts as diaphragm in both cases. A current density ranging from 1 - 7 A/dm² is applied for theoretical time viz. 8 Faradays per mole of fluorescein. Temperature is adjusted between 30 - 35°C by keeping a water bath outside the cell, the cell being a beaker of 1 litre capacity. For stationary electrode a mechanical stirrer is provided with glass stirrer. After electrolysis the solution is filtered to remove any insoluble compound and the solution neutralised to pH 2. The dye erythrosine or eosin is filtered, washed and dried.

The following typical examples of halogenation of fluorescein to erythrosine or eosin will illustrate the process of the invention, but should not be construed to limit the scope of the present invention.

EXAMPLE I

Iodination of fluorescein to erythrosine

Vol. of anolyte	: 600 ml containing 60g Na ₂ CO ₃ + 13.5g I ₂ + 10g fluorescein + 34.5g boric acid
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Vol. of catholyte	: 50ml containing 10% Na_2CO_3
Current	: 2.5A
Current density	: $3.5\text{A}/\text{dm}^2$
Anode (Rotating)	: Graphite of area 0.7 dm^2
Duration	: 3 hours
Quantity of current	
No. of amp. hours passed	: 7.5 Amp.Hrs.
Cell voltage	: 9.5 - 12 V
Temperature	: $30-40^\circ\text{C}$
Cathode	: Stainless steel of area 0.7dm^2
Diaphragm	: Ceramic porous pot
Wt. of insolubles	: 1.1g
Wt. of dye recovered	: 11.2g
Yield	: 50.45%
C.E.	: 38.3%

EXAMPLE II

Iodination of fluorescein to erythrosine

Vol. of anolyte	: 600 ml containing 60g Na_2CO_3 + 35.5g K + 10g fluorescein + 34.5g xxx boric acid
Vol. of catholyte	: 50ml containing 10% Na_2CO_3
Current	: 2.5A
Current density	: $3.5\text{A}/\text{dm}^2$
Anode (Rotating)	: Graphite of area 0.7dm^2
Duration	: 3 hours
Quantity of current	
No. of amp.hrs passed	: 7.5 Amp. hrs.

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Cell voltage	: 8 - 11V
Temperature	: 30 - 40°C
Cathode	: Stainless steel of area 0.7 dm ²
Diaphragm	: Ceramic porous pot
Wt. of insolubles	: 1.2g
Wt. of dye recovered	: 14g
Yield	: 63%
C.E.	: 47.9

EXAMPLE III

Iodination of fluorescein to erythrosine

Vol. of anolyte	: 500ml containing 50g NaHCO ₃ + 40g fluorescein + 27g + ₂
Vol. of catholyte	: 50ml containing 10% NaHCO ₃
Current	: 5A
Current density	: 7A/dm ²
Anode (Rotating)	: Lead dioxide coated graphite of are 0.7 dm ²
Duration	: 5 hours
Quantity of current No. of amp. hrs passed	: 25 Amp. hrs.
Cell voltage	: 9 - 10V
Temperature	: 30-35°C
Cathode	: Stainless steel of area 0.7dm ²
Diaphragm	: Ceramic porous pot
Wt. of insolubles	: 2.9g
Wt. of dye recovered	: 33.5g

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Yield : 40.6%
C.E. : 39 %
Wt. of iodate estimated : 10g

EXAMPLE IV

Bromination of fluorescein to eosin

Vol. of anolyte : 500ml containing 50g Na_2CO_3 + 10g
fluorescein + 20g NaBr
Vol. of catholyte : 50ml containing 10% Na_2CO_3
Current : 2.5A
C.D. : $3.5\text{A}/\text{dm}^2$
Anode (Rotating) : Graphite of area 0.7 dm^2
Duration : 3 hours
Quantity of current
No. of amp. hours passed : 7.5 Amp. hrs
Cell voltage : 7 - 9 V
Temperature : $30 - 35^\circ\text{C}$
Cathode : Stainless steel of area 0.7 dm^2
Diaphragm : Ceramic porous pot
Wt. of insolubles : Negligible
Wt. of dye recovered : 8.6g
Yield : 72.5 %
C.E. : 66.2%

EXAMPLE V

Bromination of fluorescein to eosin

Vol. of anolyte : 500ml containing 50g NaHCO_3 + 86.5g
Na Br + 40g fluorescein

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Vol. of catholyte	: 50ml containing 10% NaHCO_3
Current	: 4A
C.D.	: $5.7\text{A}/\text{dm}^2$
Anode (Rotating)	: Lead dioxide deposited graphite of area 0.7 dm^2
Duration	: 6 Hours
Quantity of current	
No. of amp. hours passed	: 24 Amp. Hrs.
Cell voltage	: 7.5 - 10V
Temperature	: 30 - 35°C
Cathode	: Stainless steel of area 0.7dm^2
Diaphragm	: Ceramic porous pot
Wt. of insolubles	: Negligible
Wt. of dye recovered	: 43.2g
Yield	: 90%
C.E.	: 82.9%
Wt. of bromate estimated	: 0.28g

EXAMPLE VI

Bromination of fluorescein to eosin

Vol. of anolyte	: 500ml containing 50g NaHCO_3 + 86.5g Na Br + 40g fluorescein
Vol. of catholyte	: 50ml containing 10% NaHCO_3
Current	: 4A
C.D.	: $5.7\text{A}/\text{dm}^2$

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Anode (Stationary)	: Lead dioxide deposited graphite of area 0.7 dm^2
Duration	: 6 hours
Quantity of current No. of amp.hours passed	: 24 Amp.Hrs
Cell voltage	: 8 - 10V
Temperature	: 30 - 35°C
Cathode	: Stainless steel of area 0.7 dm^2
Diaphragm	: Ceramic porous pot
Wt. of insolubles	: 2.9g
Wt. of dye recovered	: 31.6g
Yield	: 66.4%
C.E.	: 60.7%
Wt. of bromate estimated	: 1.5g

The following are the main advantages of the invention:

1. Since the dye obtained is a tetrahalogenated one, it does not require further purification.
2. Use of bromine which is hazardous can be avoided in the case of eosin by the above method.
3. The cost of chemicals are comparatively cheap in the above method thereby bringing down the cost of production.

Dated this *Second* Day of *September* 1987

Signed *N. R. Subbaram* Designation

N. R. SUBBARAM
(Int. Adv. of Patents)
PATENT
NEW DELHI

168346

COMPLETE SPECIFICATION

(Section—10)

Title : IMPROVED PROCESS FOR THE MANUFACTURE OF
ERYTHROCINE/EOSIN FROM FLUCRESCEIN.

Applicant : COUNCIL OF SCIENTIFIC AND INDUSTRIAL RESEARCH,
RAFI MARG, NEWDELHI-110001, INDIA an INDIAN
REGISTERED BODY INCORPORATED UNDER THE
REGISTRATION OF SOCIETIES ACT (ACT XXI OF
1860).

Inventors : PAYYALLUR NARAYANAN ANANTHARAMAN, MICHAEL
NOEL.

The following specification particularly describes and ascertains the nature of this invention and the manner in which it is to be performed :—

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This invention relates to an improved process for the manufacture of erythrocin/eosin from fluorescein. The product of this invention has wide application for use as dye in food and cosmetic industries.

Hitherto erythrocin/eosin has been prepared by chemical or electro chemical iodination/bromination of fluorescein in sodium carbonate or sodium hydroxide containing a little excess iodine/sodium bromide.

These processes have the following drawbacks:

In the electrochemical method too much iodate/bromate is formed thereby reducing the current efficiency and yield. In the chemical method the purity of the compound is affected by the formation of dihalogen compounds instead of tetrahalogen compounds thereby escalating the cost of production in the process of purification.

The object of this invention is to provide an improved process obviating these disadvantages.

According to the present invention there is provided an improved process for the manufacture of erythrocin/eosin from fluorescein which comprises halogenating an anolyte consisting of a suspension of fluorescein in an inorganic solvent selected from 10% solution of sodium bicarbonate or 10% solution of sodium carbonate with equivalent amount of boric acid alongwith iodine or sodium bromide, the catholyte being 10% solution of sodium bicarbonate or sodium carbonate in a divided cell having ceramic diaphragm, ss. cathode & graphite, lead dioxide deposited graphite or RuO_2 coated titanium anode,

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employing current density of $3.5 - 7 \text{ A/dm}^2$ at a temperature between $30-40^\circ\text{C}$ for 3-6 hrs filtering the resulting solution to remove impurities, neutralising to pH2 followed by further filtering, washing the residue with water and drying the erythrosine/eosin at a temperature below 120°C .

Lead dioxide is deposited over a smooth graphite electrode as per the data given in literature. The RuO_2 coated titanium can be obtained commercially from the company which is manufacturing ISI anodes for chlor alkali industries in the country. The electrolysis is carried out in a divided cell comprising of ceramic diaphragm and S.S. cathode, anolyte being sodium carbonate and boric acid of 10% concentration each or sodium bicarbonate of 10% concentration containing fluorescein and iodine/sodium bromide and catholyte being sodium bicarbonate of 10% concentration.

A graphite or a lead dioxide deposited graphite or RuO_2 coated titanium acts as anode and S.S. acts as cathode. The anode can be either stationary or rotating. A ceramic porous pot acts as diaphragm in both cases. A current density ranging from $1-7 \text{ A/dm}^2$ is supplied for theoretical time viz. 8 Faraday per mole of fluorescein. Temperature is adjusted between $30-40^\circ\text{C}$ by keeping a water bath outside the cell, the cell being a beaker of 1 litre capacity. For stationary electrode a mechanical stirrer is provided with glass stirrer. After electrolysis the solution is

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filtered to remove the insoluble compound and the solution neutralised to pH2 using dil H_2SO_4 . The dye erythrosine/eosin is filtered, washed and oven dried. The drying may be effected in an air oven at a temperature less than $120^{\circ}C$.

The following examples are given to illustrate the invention which should not however be construed to limit the scope of this invention.

Example I

Iodination of fluorescein to erythrosine:

Anolyte	: 500 ml water contg. 60 g Na_2CO_3 + 13.5 g I_2 + 10 g fluorescein + 34.5 g boric acid
Catholyte	: 50 ml water contg. 10% Na_2CO_3
Current	: 2.5A
Current density	: $3.5A/dm^2$
Anode	: Graphite of area $0.7 dm^2$
Duration	: 3 Hours
Qty. of current	: 7.5 amp.hrs
Cell voltage	: 9.5 - 12V
Temperature	: $30-40^{\circ}C$
Cathode	: S.S. of area $0.7 dm^2$
Diaphragm	: Ceramic porous pot
Wt. of insolubles	: 1.1 g

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Wt. of dye recovered	: 11.2g
Yield	: 50.45%
C.E.	: 38.3%

EXAMPLE II

Iodination of fluorescein to erythrosine

Anolyte	: 600ml water containing 60g Na_2CO_3 + 35.5g KI + 10g fluorescein + 34.4g boric acid
Catholyte	: 50ml water containing 10% Na_2CO_3
Current	: 2.5A
Current density	: 3.5A/dm ²
Anode(Rotating)	: Graphite of area 0.7 dm ²
Duration	: 3 hours
Quantity of current	: 7.5 amp.hrs
Cell voltage	: 8 - 11V
Temperature	: 30 - 40°C
Cathode	: S.S.area of 0.7 dm ²
Diaphragm	: Ceramic porous pot
Wt. of insolubles	: 1.2g
Wt. of dye recovered	: 14g
Yield	: 63%
C.E.	: 47.9%

EXAMPLE III

Iodination of fluorescein to erythrosine

Anolyte	: 500ml water containing 50g NaHCO_3 + 40g fluorescein + 27g I_2
Catholyte	: 50ml water containing 10% NaHCO_3
Current	: 5A
Current density	: 7A/dm ²
Anode(Rotating)	: Lead dioxide deposited graphite of area 0.7 dm ²

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Duration	: 5 hours
Qt. of current	: 25 amp.hrs.
Cell voltage	: 9 - 10V
Temperature	: 30 - 35°C
Cathode	: S.S. of area of 0.7 dm ²
Diaphragm	: Ceramic porous pot
Wt. of insolubles	: 2.9g
Wt. of dye recovered	: 33.5g
Yield	: 40.0%
Current efficiency	: 39%
Wt. of iodate estimated	: 10g

EXAMPLE IV

Iodination of fluorescein to erythrosine

Anolyte	: 500ml water containing 50gNaHCO ₃ + 40g fluorescein + 27gI ₂
Catholyte	: 100ml water containing 10% NaHCO ₃
Current	4A
Current density	: 6A/dm ²
Anode(Rotating)	: RuO ₂ coated titanium of area 0.67 dm ²
Duration	: 6 hours
Qty. of current	: 25 amp.hrs
Cell voltage	: 7 - 12V
Temperature	: 30 - 35°C
Cathode	: S.S. of area 0.7 dm ²
Diaphragm	: Ceramic porous pot
Wt. of insolubles	: 1.5g
Wt. of dye recovered	: 32.6g
Yield	36.7%
Current efficiency	: 33%
Dye content	: 92.9%(Dye content was determined by ISI method vide IS 1697-1974)

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EXAMPLE V

Bromination of fluorescein to eosin

Anolyte	: 500ml water containing 50gNa ₂ CO ₃ + 10g fluorescein + 20g NaBr
Catholyte	: 50ml water containing 10%Na ₂ CO ₃
Current	: 2.5A
Current density	: 3.5A/dm ²
Anode(Rotating)	: Graphite of area 0.7 dm ²
Duration	: 3 hours
Qty. of current	: 7.5 amp.hrs.
Cell voltage	: 7 - 9 V
Temperature	: 30 - 35°C
Cathode	: S.S. of area 0.7 dm ²
Diaphragm	: Ceramic porous pot
Wt. of insolubles	: Negligible
Wt. of dye recovered	: 8.6g
Yield	: 50%
Current efficiency	: 33%

EXAMPLE VI

Bromination of fluorescein to eosin

Anolyte	: 500ml water containing 50gNa ₂ CO ₃ + 86.5g NaBr + 40g fluorescein.
Catholyte	: 50ml water containing 10% NaHCO ₃
Current	: 4A
Current density	: 5.7A/dm ²
Anode(Rotating)	: Lead dioxide dseposited graphite of area 0.7 dm ²
Duration	: 6 Hours
Qty. of current	24 amp.hrs
Cell voltage	: 7.5 - 10V
Temperature	: 30 - 35°C
Cathode	: S.S. of area 0.7 dm ²
Diaphragm	: Ceramic porous pot

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Wt. of insolubles	: Negligible
Wt. of dye recovered	: 43.2g
Yield	: 52.6%
Current efficiency	: 59.6 %
Wt. of bromate estimated	: 0.28g

EXAMPLE VII

Bromination of fluorescein to eosin

Anolyte	: 500ml water containing 50gNaHCO ₃ + 86.5g NaBr + 40g fluorescein
Catholyte	: 50ml water containing 10% NaHCO ₃
Current	: 4A
Current density	: 5.7A/dm ²
Anode(stationary)	: Lead dioxide deposited graphite of area 0.7 dm ²
Duration	: 6 Hours
Quantity of current	: 24 amp. hrs
Cell voltage	: 8 - 10V
Temperature	: 30 - 35°C
Cathode	: S.S. of area 0.7 dm ²
Diaphragm	: Ceramic porous pot
Wt. of insolubles	: 2.9g
Wt. of dye recovered	: 31.6g
Yield	: 45.8%
Current efficiency	: 43.6%
Wt.of bromate estimated	: 1.5g

The following are the main advantages of the invention:

1. Since the dye obtained is a tetrahaloogenated one it does not require further purification.
2. Use of bromine which is hazardous can be avoided in the case of eosin by the above method.
3. The cost of chemicals are comparatively cheap in the above method thereby bringing down the cost of production.

WE CLAIM

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1. An improved process for the manufacture of erythrocin/eosin from fluorescein which comprises halogenating an anolyte consisting of a suspension of fluorescein in an inorganic solvent selected from 10% solution of sodium bicarbonate or 10% solution of sodium carbonate with equivalent amount of boric acid alongwith iodine or sodium bromide, the catholyte being 10% solution of sodium bicarbonate or sodium carbonate in a divided cell having ceramic diaphragm, ss. cathode & graphite, lead dioxide deposited graphite or RuO_2 coated titanium anode, employing current density of $3.5 - 7 \text{ A/dm}^2$ at a temperature between $30-40^\circ\text{C}$ for 3-6 hrs filtering the resulting solution to remove impurities, neutralising to pH2 followed by further filtering, washing the residue with water and drying the erythrocin/eosin at a temperature below 120°C .
2. An improved process as claimed in claim 1 wherein fluorescein employed upto 4% of the inorganic solvent used.
3. An improved process as claimed in claim 1 wherein iodine or sodium bromide added in equivalent to the quantity of fluorescein.
4. An improved process for the manufacture of erythrocin/eosin from fluorescein substantially as herein described with reference to the examples.

Dated this...^{6th}...day of...April...1988



(N.R. SUBBARAM)

JOINT ADVISER (PATENTS)

COUNCIL OF SCIENTIFIC AND INDUSTRIAL RESEARCH