

# A study of a skin patch containing two medicines (physostigmine and hyoscine) in healthy male participants to assess the blood levels of the two medicines and any associated symptoms.

<b>Submission date</b> 15/11/2018	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
<b>Registration date</b> 07/03/2019	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 08/03/2019	<b>Condition category</b> Injury, Occupational Diseases, Poisoning	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

A patch for application to the skin containing two medicines (physostigmine and hyoscine) has been developed to be worn by military and support personnel at risk of poisoning by nerve agents. The patch is designed to allow these medicines to cross the skin barrier into the bloodstream. The aim of this study was to measure the amount of physostigmine and hyoscine in the blood at different times and assess the symptoms associated with wearing the patch. The patches were applied for a 24 hour period on each of two days separated by at least one week. The study also assessed the way in which the physostigmine in the patch affected the activity of an enzyme in the blood called acetylcholinesterase (AChE).

### Who can participate?

Healthy male subjects between 18 and 40 years old were able to be considered for the study.

### What does the study involve?

Each subject wore the PHP patch for 24 hours on two occasions separated by at least one week. On each occasion blood samples were taken before and after patch application to measure the amounts of the medicines physostigmine and hyoscine. In addition the activity of the enzyme AChE was measured in these blood samples. The effects of the patch were assessed by recording the condition of the skin under the patch at set times and any unwanted symptoms that were experienced. Heart rate, blood pressure and electrical activity of the heart (ECG) were also recorded at set times.

### What are the possible benefits and risks of participating?

There were no direct individual benefits for the subjects participating. However, the information collected from these individuals added to the scientific knowledge about the PHP patch. All medicinal products have a risk of causing side effects. The most common side effects known

about for the PHP patch and seen in this study were itching and redness at the sites on the arm where the patch was applied. Some subjects also experienced a feeling of sickness and some had disturbed sleep.

Where is the study run from?

The study was run at one clinical research centre, Simbec Research Limited.

When is the study starting and how long is it expected to run for?

The study started in February 2014 and ended in June 2014.

Who is funding the study?

The Defence Science and Technology Laboratory.

Who is the main contact?

Defence Science and Technology Laboratory  
centralenquiries@dstl.gov.uk

## Contact information

**Type(s)**

Public

**Contact name**

Dr Medical Advisor

**Contact details**

Dstl  
Porton Down  
United Kingdom  
SP4 0JQ

## Additional identifiers

**Clinical Trials Information System (CTIS)**

2012-004428-39

**ClinicalTrials.gov (NCT)**

N/A

**Protocol serial number**

RD 209/25394

## Study information

**Scientific Title**

An open, replicate, two-period, single and multiple-dose, pharmacokinetic and tolerability study of the PHP (150 g/m<sup>2</sup>) transdermal patch containing physostigmine and hyoscine in healthy, adult Caucasian males.

**Acronym**

N/A

### **Study objectives**

The PHP 150 g/m<sup>2</sup> transdermal patch is safe and well tolerated and has appropriate pharmacokinetic and pharmacodynamics profiles.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Approved 12/10/2013, Ministry of Defence Research Ethics Committee (MoDREC), ref: 384/PPE/12.

### **Study design**

Open-label replicate single-dose study

### **Primary study design**

Interventional

### **Study type(s)**

Prevention

### **Health condition(s) or problem(s) studied**

Potential risk of poisoning by nerve agent

### **Interventions**

Each subject received 2 single applications of a transdermal patch containing physostigmine and hyoscine (150 g/m<sup>2</sup>) worn with an armband for 24 h over 2 periods (one application/period).

### **Intervention Type**

Drug

### **Phase**

Phase I

### **Drug/device/biological/vaccine name(s)**

Physostigmine, hyoscine

### **Primary outcome(s)**

Plasma PK and intra-subject PK variability of physostigmine and hyoscine after single and multiple dosing of the PHP (150 g/m<sup>2</sup>):

1. Plasma concentrations of physostigmine measured at: Plasma PK at pre-determined times throughout both period 1 and period 2- Day 1 pre-dose, 3, 6, 9, 12, 15, 18, 21, 24 (Day 2), 27, 30, 33, 36, 39, 48 (Day 3), 72 (Day 4), 96 (Day 5) and follow-up (168 (Day 8) h post-dose). Assay method-liquid chromatography tandem mass spectrometry (LC-MS/MS) assay.
2. Plasma concentrations of hyoscine measured at: Plasma PK at pre-determined times throughout both period 1 and period 2 - Day 1 pre-dose, 3, 6, 9, 12, 15, 18, 21, 24 (Day 2), 27, 30, 33, 36, 39, 48 (Day 3), 72 (Day 4), 96 (Day 5) and follow-up (168 (Day 8) h post-dose). Assay method-liquid chromatography tandem mass spectrometry (LC-MS/MS) assay.

### **Key secondary outcome(s))**

The local tolerability of the PHP (150 g/m<sup>2</sup>) transdermal patch and its PD profile were measured using the assay method-spectrophotometric method to measure red cell acetylcholinesterase (AChE) activity. Activity was measured at pre-determined times throughout both period 1 and period 2- at baseline (Day -1 and Day 0), Day 1 pre-dose, 3, 6, 9, 12, 15, 18, 21, 24 (Day 2), 27, 30, 33, 36, 39, 48 (Day 3), 72 (Day 4) and follow-up (168 (Day 8) h post-dose).

**Completion date**

04/06/2014

## Eligibility

**Key inclusion criteria**

1. Able to give written informed consent prior to study participation
2. Healthy Caucasian male participants aged 18-40 years (inclusive).
3. Body mass index (BMI) within the range of  $\geq 19$  and  $\leq 30$  kg/m<sup>2</sup>.
4. Supine vital signs with no clinically significant deviations outside the following ranges:
  - 4.1. Heart rate 40-90 bpm
  - 4.2. Systolic blood pressure 90-140 mmHg
  - 4.3. Diastolic blood pressure 50-90 mmHg
5. Agreement not to attempt to father a child during the study or for 3 months after treatment. Participants with a partner who could become pregnant must have agreed to use a reliable form of contraception during the trial and for 3 months afterwards, e.g. condom, established use of oral, injected or implanted hormonal contraceptive, intra-uterine device, diaphragm with spermicide.
6. Able to communicate well with the Investigator and to comply with the requirements of the study.

**Participant type(s)**

Healthy volunteer

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Upper age limit**

40 years

**Sex**

Male

**Total final enrolment**

35

**Key exclusion criteria**

1. Presence of any clinically significant medical condition as determined by the Investigator
2. Any surgical or medical condition which might have significantly altered the absorption, distribution, metabolism or excretion of any drug (e.g. renal or liver disease, respiratory, immunological, endocrine or neurological disorders)
3. Any ECG abnormality considered to be clinically significant i.e. prolongation of QT/QTc interval >450 msec or history of additional risk factors for Torsades de Point (heart failure, hypokalemia, family history of long QT syndrome)
4. Known or suspected hypersensitivity or idiosyncratic reaction to any of the study products
5. History of asthma (within the previous 10 years), exercise-induced bronchospasm or relevant seasonal bronchospasm
6. Lung function of less than 80% of predicted forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC)
7. Any history of contact dermatitis
8. Any skin disorder, broken skin, scars, tattoos at the sites of patch application (i.e. on both upper arms)
9. Glaucoma or a history of glaucoma in first-degree relatives (i.e. parents, siblings or offspring)
10. Presence of anterior chamber narrow angle (Van Herrick Grade 1 and 2)
11. Intraocular pressure exceeding 20 mmHg
12. Contact lens wearer
13. History or evidence of drug abuse (opiates, methadone, cocaine, amphetamines, cannabinoids or barbiturates)
14. Positive urine test for alcohol (test could have been repeated at baseline (Day -1 and Day 0), at the Investigator's discretion)
15. History or evidence of alcohol abuse defined as an intake of more than 28 units per week where 1 unit corresponds to 250 ml beer, 20 ml spirits/liqueur or 100 ml of wine
16. Participation in a new chemical entity (NCE) clinical study within the last 4 months or a marketed drug clinical study within the previous 3 months. (N.B. Washout period between studies defined as the period of time elapsed between the last dose of the previous study and the first dose of the next study.)
17. Use of any prescription medication within the last 14 days
18. Use of non-prescription medication (apart from paracetamol and ibuprofen) within the last 7 days that may have impacted on the safety and objectives of the study (at the Investigator's discretion)
19. Donation of blood or blood products within the last 3 months, or the intention to donate blood or blood products within 3 months after completion of the study

**Date of first enrolment**

11/02/2014

**Date of final enrolment**

04/06/2014

## **Locations**

**Countries of recruitment**

United Kingdom

Wales

**Study participating centre**  
**Simbec Research Ltd**  
Merthyr Tydfil  
Merthyr Tydfil  
United Kingdom  
CF48 4DR

## Sponsor information

### Organisation

Dstl

### ROR

<https://ror.org/04jswqb94>

## Funder(s)

### Funder type

Government

### Funder Name

Ministry of Defence

### Alternative Name(s)

MOD

### Funding Body Type

Government organisation

### Funding Body Subtype

National government

### Location

United Kingdom

## Results and Publications

### Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are not expected to be made available due to lack of original subject consent.

### IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes