

A programme to develop a skin patch containing two medicines (physostigmine and hyoscine), Study 7: Assessment of effects of an armband covering the skin patch on the blood levels of the two medicines and any associated symptoms in healthy male participants

Submission date 17/12/2020	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
Registration date 11/01/2021	Overall study status Completed	<input type="checkbox"/> Protocol
Last Edited 18/12/2020	Condition category Injury, Occupational Diseases, Poisoning	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

A skin patch containing two medicines (physostigmine and hyoscine) has been developed. The skin patch releases these medicines enabling them to cross the skin into the bloodstream. The aim of this study was to measure the effect of an armband applied over the F11/21 transdermal patch (area 21 cm²) on the amount of physostigmine and hyoscine delivered to the blood at different times. The participants in the study were healthy male participants.

Who can participate?

Study participants were males aged between 18 and 40 years.

What does the study involve?

Each participant wore a F11/21 transdermal patch for 24 hours on four separate occasions. There was a 7-day gap between each patch application. On two of the four occasions the patch was worn with an armband covering the patch, and on the other two occasions it was worn without one.

Blood samples were taken before and after patch application to measure the amounts of the two medicines (physostigmine and hyoscine). In addition the activity of the enzyme acetylcholinesterase was measured in these blood samples. The condition of the skin under the patch was recorded at set times and any symptoms experienced while it was worn were noted. Heart rate, blood pressure, electrical activity of the heart (ECG), tests of vision and cognitive function were also recorded at set times.

What are the possible benefits and risks of participating?

There were no direct benefits for the individuals participating in this study. However, the

information collected from the study will add to the scientific knowledge about the physostigmine and hyoscine patch. All medicinal products may cause side effects. The most common side effects known about the medicines in the patch are nausea and vomiting due to physostigmine and blurred vision and dry mouth due to hyoscine. Application of the F-11/21 patch with and without an armband was considered to be well-tolerated.

Where is the study run from?

The study was conducted at Simbec Research Limited (UK).

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

December 2007 to February 2011

Who is funding the study?

Ministry of Defence (UK)

Who is the main contact?

Defence Science and Technology Laboratory, Porton Down
centralenquiries@dstl.gov.uk

Contact information

Type(s)

Scientific

Contact name

Dr Medical Advisor

Contact details

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Additional identifiers

Clinical Trials Information System (CTIS)

2008-000503-28

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number

RD 209/24679

Study information

Scientific Title

An investigation of the effects of an armband applied over the F11/21 physostigmine and hyoscine transdermal patch on pharmacokinetic, pharmacodynamic and safety profiles in healthy male subjects

Study objectives

The aim of the study was to assess the effect of the armband on the pharmacokinetic (PK) and pharmacodynamic (PD) profiles of physostigmine and hyoscine during 24h transdermal administration in healthy male subjects.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 06/03/2008, South East Wales Local Research Ethics Committees (LREC) (Churchill House, 17 Churchill Way, Cardiff, CF10 2TW, UK; +44 (0)2920 402402; no email provided), ref: 08 /WSE04/21

Study design

Single centre open label randomized within-subject replicate crossover study

Primary study design

Interventional

Study type(s)

Other

Health condition(s) or problem(s) studied

Potential risk of poisoning by nerve agent

Interventions

Generic drug name- physostigmine and hyoscine (transdermal patch)
Dosage - a single 24-hour application of active 21cm² patch formulation F-11 (F21/21) administered on 4 separate occasions with a 7- day interval between applications.

Randomisation

Subjects were allocated to one of six treatment sequences according to a randomisation code produced by the CRO.

Intervention Type

Drug

Phase

Phase II

Drug/device/biological/vaccine name(s)

Physostigmine, hyoscine

Primary outcome(s)

1. Physostigmine and hyoscine plasma measured at pre-dose and regular intervals up to 54 hours after patch application. Assay- by liquid chromatography-tandem mass spectrometry (LC-MS-MS)

method

2. Acetylcholinesterase levels measured at baseline, pre-dose, and intervals up to 54 hours after patch application. The method was validated spectrophotometric method

Key secondary outcome(s)

Safety and tolerability of the F11/21 transdermal patch worn with and without an armband:

1. Vital signs and ECG were measured at screening, pre-dose, up to 54 hour after patch application and at follow up
2. Ocular function (near point and accommodation) was measured at screening, pre-dose, up to 54 hours after patch application
Patch application site assessment was made at screening, baseline, and up to 48 hours after each patch application
3. Self-reported symptoms of nausea (attributed to relative physostigmine excess) or blurred vision (attributed to relative hyoscine excess) up to 54 hours after patch application

Completion date

15/02/2011

Eligibility

Key inclusion criteria

1. Ability to give written informed consent prior to study participation
2. Healthy Caucasian male subjects aged between 18 and 40 years (inclusive)
3. Body Mass Index (BMI) within the range of ≥ 21 and ≤ 29 kg/m²
4. Vital signs within 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. Ability 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

Sex

Male

Total final enrolment

31

Key exclusion criteria

Screening:

1. Presence of any clinically significant medical condition as determined by the Investigator
2. Any surgical or medical condition which might significantly alter 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. baseline prolongation of QT /QTc interval >450 ms or history of additional risk factors for Torsade 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. A dibucaine number of less than 70
6. History of asthma (within the previous 10 years), exercise induced bronchospasm or relevant seasonal bronchospasm
7. Lung function of less than 80% of predicted FEV1 and FVC
8. Any history of contact dermatitis
9. Any skin disorder, broken skin, scars, tattoos at the sites of patch application (i.e. on both arms)
10. Glaucoma or a history of glaucoma in first-degree relatives (i.e. parents, siblings or offspring)
11. Presence of Anterior Chamber Narrow Angle (Van Herrick Grade 1 and 2)
12. Intra-ocular pressure exceeding 20 mmHg
13. Uncorrected vision in both eyes of worse than 6/9 on the Snellen Scale
14. Corrected vision of 6/9 or better on the Snellen Scale when wearing +2.25 dioptre reading glasses
15. Required glasses or contact lenses for distance vision
16. History or evidence of drug abuse (opiates, methadone, cocaine, amphetamines, cannabinoids or barbiturates)
17. Positive test for HIV, hepatitis B or hepatitis C
18. History or evidence of alcohol abuse defined as an intake of more than 28 units per week (4 units per day), where 1 unit corresponds to 250 ml beer, 20 ml spirits/liqueur or one glass (100 ml) of wine
19. Positive urine test for alcohol
20. Participation in another clinical study within the last three months
21. Use of any prescription medication within the last 14 days
22. Use of non-prescription medication (apart from paracetamol) within the last seven days that may have an impact on the safety and objectives of the study (at the Investigator's discretion)
23. Donation of blood or blood products within the last three months, or the intention to donate blood or blood products within three months after completion of the study

Baseline (all periods):

1. Development of any exclusion criteria since last visit
2. Positive urine test for alcohol
3. Positive drugs of abuse test
4. Use of any prescription medication since last visit (with the exception of hormonal contraception)
5. Use of non-prescription medication that may impact the safety aspects and objectives of the study, within the last seven days (apart from paracetamol)

Date of first enrolment

06/03/2008

Date of final enrolment

10/11/2008

Locations

Countries of recruitment

United Kingdom

Wales

Study participating centre

Simbec Research Limited

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Merthyr Tydfil

United Kingdom

CF48 4DR

Sponsor information

Organisation

Defence Science and Technology Laboratory

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 confidentiality.

IPD sharing plan summary

Not expected to be made available