Introduction to physiology and pharmacology

The aim of this experiment is to prepare a sample of guinea pig ileum and to determine the contractile “ dose response curve to acetylcholine” and “ dose response curve to carbachol and biological variation”.

Abstract

In this experiment pharmacological effect of acetylcholine and carbachol are studied by using an isolated tissue preparation, which is a guinea pig ileum. The contractile property of the smooth muscle is used for the straightforward measurement of the force it produces as an indication of effect.

The ileum is a part of the intestines among the pyloric sphincter and colon. The ileum has a tube of muscle and epithelial layers, innervated by bundles of fibres. The muscle layers have inherited contractility. The contractility is transformed by the nervous inputs in the myenteric plexuses. In the myenteric plexuses the ganglia linking pre and post ganglionic neurons with acetylcholine act to transmit among them. The muscle layer makes the tissue shorter and pulls the tube together. So the muscle lengthens the tissue little bit. Acetylcholine can stimulate the contraction when it is released from the enteric nerve terminals onto the muscle layers. In the enteric nervous system are the muscarinic g-protein coupled receptors. Those receptors mediate a biological response an acetylcholine agonist. The cells of the muscle form gap junctions with each other and so are electrically coupled, allowing for smooth coordinated contractions that underlie peristalsis.

The ileum was kept continually in the oxygenated Tyrode’s solution. The temperature of Tyrode solution was maintained at 32 Celsius. The

contraction or relaxation of the piece of tissue was attached to an isotonic transducer. An instrument, which converted changes into electrical current and that, was used to drive a pen recorder.

Method:

For the second experiment the time was reduced to 4 minutes from 8 minutes.

Description of the results

Acetylcholine

Average % Max Response

Dose

Response Height

Percentage Maximum Response

Test 1

Test 2

Test 3

Test 1

Test 2

Test 3

A

0. 00000001

0. 00

0. 00

0. 00

0. 00

0. 00

0. 00

0. 00

B

0. 00000003

0. 00

1. 00

45. 00

0. 00

0. 87

10. 47

3. 78

C

0. 00000010

1. 00

10. 00

85. 00

1. 00

8. 70

19. 77

9. 82

D

0. 00000030

3. 50

115. 00

220. 00

3. 50

100. 00

51. 16

51. 55

E

0. 00000100

100. 00

110. 00

430. 00

100. 00

95. 65

100. 00

98. 55

F

0. 00000300

80. 00

100. 00

380. 00

80. 00

86. 96

88. 37

85. 11

Carbachol

Average % Max Response

Dose

Response Height

Percentage Maximum Response

Test 1

Test 2

Test 3

Test 1

Test 2

Test 3

A

0. 00000001

40. 00

20. 00

0. 00

3. 28

3. 23

0. 00

2. 17

B

0. 00000003

20. 00

20. 00

0. 00

1. 64

3. 23

0. 00

2. 15

C

0. 00000010

240. 00

100. 00

5. 00

19. 67

16. 13

5. 26

13. 69

D

0. 00000030

280. 00

170. 00

40. 00

22. 95

27. 42

42. 11

30. 83

E

0. 00000100

560. 00

620. 00

80. 00

45. 90

100. 00

84. 21

76. 70

F

0. 00000300

1220. 00

540. 00

95. 00

100. 00

87. 10

100. 00

95. 70

Discussion

A more sophisticated organ bath could be used as the volume of the bath was filled visually. If it had a mark then the filled amount would be the same and no error would occur.

Questions:

The ileum is innervated by the enteric, sympathetic and parasympathetic divisions of the autonomic nervous system.

The Myenteric (Auerbach's) and submucosal (Meissner's plexuses) are the two plexuses of the enteric nervous system.

The agonists Histamine and ATP cause peristaltis in the gut. (Morphin, cannabis drugs)

A vehicle is a pharmaceutical ingredient (usually a liquid) used a medium for dissolving the active drug in a mass suitable for its administration. The transporting agent is used to increase the bulk or decrease the concentration of a mixture.

Acetylcholine esterase cannot easily metabolise carbachol.

Carbachol is a choline ester and does not well absorb in the gastrointestinal tract. It does not cross the blood brain barrier.

Carbachol is a drug that binds and activates the acetylcholine receptor. It is classified as a cholinergic agonist. Applications are for ophthalmic purpose, such as treating glaucoma or for use during ophthalmic surgeries. It stimulates bladder emptying and for chemotherapy induced nausea and vomiting. Postradiation nausea and vomiting.

Yes, the dose range for each agonist is sufficient to obtain a complete dose response curve. Both agonists reached a maximum response.

EC50 11

No difference 12

13

14

15

Antiemetic can either reduce nausea or stop people from throwing up. Different drugs types and different strength are in use. The simplest indication is and simple motion sickness and to prevent nausea or for nausea. They antagonize the following receptors :

1-peripheral 5-HT3 receptor blockade on intestinal vagal afferents; 2-central5-HT3 receptor blockade in the vomiting center and chemo trigger zone. Use: because of the 5HT3 receptor antagonists in the chemotherapy it is inducing vomiting.

Conclusion:

Using tissues helps to overcome some problems. If a whole guinea pig is used applying orally a drug, it may complicate the interpretation of the observations. As a tissue is used in this experiment the following factors, such as absorption from the gut and its distribution throughout the body do not have to be considered when the response of a piece of isolated tissue is controlled.

Agonists produce a biological response when applied to a tissue. From this experiment practically I gained that the produced size of response by an agonist depends on the dose. Each drug has a threshold dose. Under this dose no response can be spotted. Increasing the application of the drug over the threshold dose increases the response until it reaches a maximum value. Apart from the increased dose, the response will not increase.

Using the term concentration made the comparison between the experiments easier.

All the tissues from an animal (in this case guinea pig) may possibly response different to given drugs and make a respond from an amount of different tissues. The response from the guinea pig to acetylcholine and carbachol induced by fixed concentration different levels due to the biological variation.