Drug action on gut motility biology essay

Describe and explain the effect of field stimulation on ileum contraction? The experiment aims to determine the functional role of different drugs like morphine, atropine or naloxone on contraction of guinea pig ileum using transmural stimulation or acetylcholine applied exogenously.

The transmural stimulation is given with an initial pulse width of 0. 5ms, frequency 0. 1Hz and gradually increasing the voltage until we get a measurable contraction.

The transmural stimulation, given to the guinea pig ileum acts on enteric nervous system lining the gastrointestinal system controlling GIT , produces an action potential at the membrane causing depolarisation and permeable to calcium (ca+2) ion and leads to increase in ca+2 ion concentration through voltage gated ca +2 channel. This causes release of acetylcholine (ACh) at synaptic cleft, which are directed to bind with muscuranic (M3) receptors. These act by G- protein couple receptors mechanism. Gs – Protein activates phospholipase C (PLC), catalysis the hydrolysis of phosphoinositides, (the phospholipids found within the cell membrane) generates two second messengers inositol-1, 4, 5-triphosphate (IP3) and diacylglycerol (DAG). These second messengers, influence the protein phosphorylation and effectively regulates the intracellular ca+2 concentration. The IP3 formed binds with the IP 3 receptor and control the release of ca+2 from intracellular store. The DAG mainly activates membrance-bound protein kinase, protein kinase C (PKC) , have vast cellular distribution and phosphorylate different proteins and become reason for raised intracellular ca+2 concentration causing contraction. These two second messengers initiate the contraction of ileum by field stimulation.

2 . a . Molar concentration morphine Vs contractile response of field stimulated tissue (in mm)

Table showing the contractile response (mm) of morphine on field stimulated guinea pig ileum at different molar concentrations

Concentration of Morphine (M)

Contractile response (mm)

1 -10-10

92

3 -10-10

91

1 -10-9

90

3 -10-9

88

1 -10-8

82

3 -10-8

64

1 -10-7

36

3 -10-7

30

1 -10-6

27

3 -10-6

26

1 -10-5

24

Fig . a. showing the effect of different concentrations of morphine on guinea pig ileum measuring contractile response in mm

b. The logarithm of the molar concentration morphine Vs contractile response of field stimulated tissue (in mm)

Table showing the different contractile response at varying logarithm of molar concentration of morphine on guinea pig ileum

Log Concentration of Morphine (M)

Contractile response (mm)

-10

92

-9. 522878745

91

-9

90

-8. 522878745

88

-8

82

-7. 522878745

64

-7

36

-6. 522878745

30

-6

27

-5. 522878745

26

-5

24

Fig. b. Graph showing the effect of log concentration of morphine on guinea pig ileum measuring contractile response (in mm)

c. Molar concentration morphine Vs % relaxation of stimulated tissue.

Table showing, the % relaxation of stimulated tissue at different molar concentration of morphine.

Concentration of Morphine (M)

Percentage relaxation of stimulated tissue (%)

1 -10-10

0

3 -10-10

1. 086

1 -10-9

2. 222

3 -10-9

4. 347

1 -10-8

11. 111

3 -10-8

30. 434

1 -10-7

60. 869

3 -10-7

67. 391

1 -10-6

70. 652

3 -10-6

71. 739

1 -10-5

73. 913

Fig. c . Graph showing the % relaxation of stimulated tissue of guinea pig ileum at different molar concentration of morphine.

d. Molar concentration of acetylcholine Vs contractile response in unstimulated tissue (in mm)

Table showing the contractile response of unstimulated tissue (in mm) at different molar concentration of acetylcholine (M)

Molar concentration of Ach (M)	Contractile Response (mm)
1 -10-8	17
3 -10-8	37
1 -10-7	49
3 -10-7	58
1 -10-6	59
3 -10-6	59

Fig. d. Graph showing the contractile response (in mm) on unstimulated tissue of guinea pig ileum at different concentration of acetylcholine

e. The logarithm of the molar concentration acetylcholine Vs contractile response in unstimulated tissue (in mm)

Table showing, contractile response (in mm) of unstimulated tissue at different concentrations of acetylcholine.

Log Concentration of acetylcholine (M)

Contractile Response (mm)

-8

17

-7. 522878745

37

-7

49

-6. 522878745

58

-6

59

-5. 522878745

59

Fig. e. Graph showing contractile response (in mm) of unstimulate tissue of guinea pig ileum at different log concentration of morphine.

3. Explain the effects of morphine on field stimulated-induced contractions and how/why this is affected by atropine and naloxone?

Morphine is an opioid analgesic drug acts on opioid receptors. There are three major subgroups under opiod receptors: μ (mu), δ (delta) and κ (kappa) receptors. Morphine mostly acts on μ receptors.

From the graph, during field stimulation-contraction, on addition of morphine of 0. 1nM concentration it does not show any much effect initially, but on increasing concentration of morphine it shows gradual decrease in contractile response and sudden downfall of response by half from 100nM to 300nM and then stabilise with little varying response (in mm) in further concentration.

This is due to, when morphine is added to the bath of field stimulated-induced contraction the activation of opioid receptors (μ), via Gi- protein, which inhibits adenyly cyclase, thus decrease in cAMP formation, leading to closing of ca+2 channels and decrease in muscle contraction by inhibting release of ACh at synaptic region.

Naloxone acts as competitive antagonist at μ, δ, κ receptors. It is also used as counter the overdose of opioid molecules.

When naloxone is added to the field stimulated guinea pig ileum, which is having morphine of certain dose causing dose-dependent decrease in response. The naloxone, acts as competitive antagonist of morphine which replaces the morphine occupied at opioid receptors and reduces the available receptors for morphine to bind and leads to reversing the morphine effect towards field-stimulated contraction. So, the response increases gradually with increase in concentration of naloxone from 200nM to 1000nM and then 3000nM. This shows effective competitive antagonism of naloxone towards morphine activity.

In case of atropine, the graph shows, on addition of atropine there is a slightly decrease in response initially and then gradually fall in response due to action of atropine as antagonist at Ach receptor, which occupies the M3 receptor and inhibits the contraction via G-protein receptor mechanism.

4. Explain the observed effects of morphine, naloxone and atropine an Ach-induced contractions and relate this to the effects on field stimulation.

From the graph, we know that the morphine and naloxone do not show much significant effect on ACh-induced contraction on guinea pig ileum than field stimulated contratcion. But the atropine show a significant effect on ACh-induced contraction.

During field stimulation, the morphine acts via Gi – protien (adenyly cylase inhibition) and inhibits cAMP formation and decrease ca+2 concentration and effect the ACh release at synaptic cleft (endogenous). But in the ACh-induced contraction, ACh is available exogenous to occupy the M3 receptors and

intiate contraction, showing morphine does not much effect its action as in graph it slightly inhibits just 0. 4mm.

Naloxone, act as opioid receptor antagonist, may not act on Muscarinic receptors, show no much effect on ACh-induced contraction as ACh in exogenous can direct act on M3 receptors as in graph and which is different in case of field stimulated contratile response, inhibits the morphine action and increases ACh at synaptic region producing significant contraction.

Atropine, is a muscarinic (M3) receptor antagonist, the graph shows a significant effect on ACh-induced contractions by atropine. Atropine as competitive antagonist, added to bath occupies the M3 receptors much faster than ACh and inhibits its action, which inturn inhibits ileum contraction.