ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

https://ijpp.com

Indian Journal of Physiology and Pharmacology

Original Article

Capsaicin fails to produce changes in contractile tension in large gut of neonate rats

Shuchita Singh[1], Parul Sharma[1], Devarshi Dixit[1], Maloy B. Mandal[1]

[1]Department of Physiology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India.

***Corresponding author:**
Parul Sharma,
Department of Physiology,
Institute of Medical Sciences,
Banaras Hindu University,
Varanasi, Uttar Pradesh, India.

drparulsharmajpr@gmail.com

Received : 16 September 2022
Accepted : 25 November 2022
Published : 29 March 2023

DOI
10.25259/IJPP_437_2022

Quick Response Code:

ABSTRACT

Objectives: Capsaicin, the most pungent constituent of chilli pepper (*Capsicum annuum* L.), is known to alter the physiological activity of the gut. Capsaicin mediates its action through a transient receptor potential vanilloid type 1 (TRPV1) channel. The action of capsaicin on gut smooth muscle varies from segment to segment in different species. The earlier studies were carried out in adult animals only, and its status in the neonate gut, which is in a development stage, is not known. Objective: Therefore, the present study was done to assess the effect of capsaicin on the large gut of neonates.

Materials and Methods: In an organ bath preparation, isometric contractions were recorded from segments of dissected rat colon and rectum. The gut segments were exposed to cumulative concentrations of capsaicin (0.01 nM–3 μM) and a capsaicin-induced contractile response was observed. TRPV1 receptor antagonist capsazepine (1 μM) and a nitric oxide synthase inhibitor, L-NAME (100 μM), were used to assess their blocking effect on capsaicin-induced contractile response.

Results: Capsaicin raised contractile tension in the colon and rectum of adult rats but not in neonate rats. In adult rats, capsazepine pre-treatment (1 μM) failed to block the capsaicin-induced response in the colon, but in the lower concentrations, it increased contractile tension in the rectum. Pre-application of L-NAME (100 μM) potentiated capsaicin-induced response in the adult rectum and neonate's colon but had no effect in the neonate rectum and adult colon. Capsaicin with a low concentration (0.01 nM–0.01 μM) increased contractile frequency in both the colon and rectum of adult rats. However, the effect of capsaicin on frequency was abolished at higher concentrations (0.01 μM–3 μM). A capsaicin-evoked change in contractile frequency in adult rats was blocked by capsazepine and L-NAME. At lower concentrations (0.01 nM–0.01 μM), capsaicin did not show any change in frequency in the neonatal colon, while a decrease in contractile frequency was observed with the higher concentrations (0.1 μM–3 μM) of capsaicin. In neonates, capsazepine pre-treatment produced changes in frequency for both the colon and rectum. However, pre-application of L-NAME decreased frequency in the neonate rectum but not in the colon.

Conclusion: Capsaicin-induced changes in contractile activity may or may not involve TRPV1 or the Nitric Oxide (NO) pathway, depending on the part of the large gut and developmental maturity.

Keywords: Capsaicin, Colon, Rectum, Gut contractility, Capsazepine

INTRODUCTION

Out of different forms of capsaicinoids, capsaicin is the primary capsaicinoid and most pungent constituent of chilli peppers (*Capsicum annuum* L.). Capsaicin is the main ingredient responsible for the spiciness of any type of food.[1] Capsaicin is known to alter the physiological activity of the gut. For example, it may change the movement, secretary and circulatory functions of the

gut as well as be involved in visceral nociception in different species.[2-4] Capsaicin may also alter gastric emptying time in humans and it is also implicated in irritable bowel syndrome.[5-9] Thus, the capsaicin receptor has turned out to be a striking target for the management of colonic and rectal disorders. Capsaicin mediates its action through the capsaicin receptor and transient receptor potential vanilloid type 1 (TRPV1) channel, which was first identified and cloned in rats by Caterina *et al*.[10] Apart from capsaicin, TRPV1 is also notably activated by changes in pH (<5.9), high temperature (>43°C) and inflammatory pain.[10-14]

Capsaicin was reported to affect the motility of the gastrointestinal tract as capsaicin receptor TRPV1 expression was observed in the mucosa, submucosal layer and muscular layer of the gastrointestinal tract in the guinea pig, mouse and rat gastrointestinal tracts.[15,16] Capsaicin has different effects on the smooth muscle of the gut in different parts of different species.[15,17-19] Capsaicin has been shown to cause biphasic responses (contractions followed by relaxation) in the ileum of guinea pigs as well as the small and large intestines of mice, possibly through substance P, tachykinin and TRPV1.[2,16-18,20-24] In addition, relaxation in the rat ileum, mouse colon, human ileum, human appendix and human sigmoid colon in response to capsaicin involved the NO pathway.[18,19,25] Thus, capsaicin is likely to mediate its action through the TRPV1 pathway or a TRPV1 independent pathway among different species.

These studies were carried out in adult animals only and its status in the neonate gut, which is in a development stage, is not known. Therefore, the present study was carried out to assess the effect of capsaicin on the large gut of neonates. This should contribute to a better understanding of the mechanism of neonate gut motility and address the issues associated with neonatal large gut motility disorders.

MATERIALS AND METHODS

Adult albino rats of the Charles Foster strain of 4–6 months and neonates of 10–16 days of the same strain were used. The animals were housed in a temperature, humidity and light-controlled room (12 h light and 12 h dark) with an ad libitum supply of food and water. The animal experiments were performed as per the guidelines of the Institutional Ethical Clearance Committee for animal experiments (No. Dean/12-13/CAEC/32). The date of ethics approval for this study is 30.06.2012.

Mounting and recording of contractile response

The detailed procedure of mounting and recording was as described earlier.[26,27] In brief, adult rats were killed by cervical dislocation and exsanguination, while neonates were by decapitation. The abdomen was opened immediately by vertical incision and part of the gut (colon and rectum) was dissected out and cleaned by flushing out the gut contents and placed in a Petri dish containing chilled Krebs-Ringer solution bubbled with 100% O_2. After cleaning, longitudinal segments (12–15 mm) of colon and rectum were dissected out and placed in an organ bath (12 mL) containing Krebs-Ringer solution maintained at 37 ± 1°C and continuously bubbled with 100% O_2. The gut segments were mounted vertically. One end of the tissue was fastened to a glass tube support and the other end was fixed to a force transducer (MLT 0210, AD Instruments, Sydney, Australia) with an initial tension of 0.25–0.5 g. In an organ bath preparation, isometric contractions were recorded from segments of dissected rat colon and rectum. The preparations were allowed to equilibrate (stabilisation) for 30 min before taking the control recordings. Isometric contractions were amplified by a bridge amplifier and digitised through an analogue/digital interface (Power Lab 4/ST system) to be acquired onto a personal computer. The contraction recording was displayed and analysed with the help of software Chart-5 for Windows (AD Instruments, Sydney, Australia). Before as well as after recording of the contractile responses, calibration for the tension (0–10 g) was performed. After stabilisation, the initial recordings of spontaneous contractions were made for 30 min at 37°C. Subsequently, the gut segments were exposed to different concentrations of capsaicin (0.01 nM–3 μM) cumulatively. Antagonists such as capsazepine (1 μM) and L-NAME (100 μM) were used to assess their blocking effect on capsaicin (0.01 nM–3 M)-induced contractile response.

Following the recording of contractions, the segment of tissue was removed from the organ bath and placed on blotting paper to lightly soak up any excess water. The two ends of the tissue were cut to remove the injured parts. The wet tissue was then weighed in a fine balance. The contractile response was expressed per unit weight of tissue (g/g wet tissue).

Drugs and solutions

The Krebs-Ringer solution was prepared with the following compositions (in mM/L): Sodium chloride (NaCl), 119; Potassium chloride (KCl), 4.7; Calcium chloride dihydrate ($CaCl_2.2H_2O$), 2.5; Potassium dihydrogen phosphate (KH_2PO_4), 1.2; Magnesium sulphate heptahydrate ($MgSO_4.7H_2O$), 1.2; Sodium bicarbonate Sodium bicarbonate ($NaHCO_3$), 5 and glucose, 11 and the pH of the solution was 7.4.

A stock solution (1 mM) of capsaicin and capsazepine was prepared in absolute alcohol. In distilled water, a 10 mM stock solution of N-nitro-L-arginine methyl ester (L-NAME) hydrochloride was prepared. Further, dilution was made in Krebs-Ringer solution before experiments.

Experimental protocol

The experiments were carried out in three groups for each adult and neonate rat. In the first group of experiments, after obtaining an initial recording of spontaneous contractions from the colon and rectum of adult ($n = 6$) and neonate ($n = 6$) rats, the tissue was subjected to treatment with each concentration of capsaicin (0.01 nM, 0.1 nM, 1 nM, 0.01 μM, 0.1 μM, 1 μM and 3 μM) for 10 min in a cumulative manner to obtain the dose-response curve. In the second group (n = 4–6), after obtaining initial recordings of spontaneous contractions from the colonic and rectal tissue of adult and neonate rats, the tissue was exposed to various volumes of ethanol (0.001–100% v/v) that is present in the corresponding concentration of capsaicin solution.

In the third group, after obtaining initial recordings of spontaneous contractions from the colonic and rectal tissue of adult and neonate rats, they were pre-treated with capsazepine (1 μM, n = 4–6) and L-NAME (100 μM, n = 4–6), then, the recordings were obtained in their presence for 10 min. Subsequently, the cumulative concentration response of capsaicin (0.01 nM–3 μM) was performed in the presence of capsazepine and L-NAME.

RESULTS

Effect of capsaicin (0.01 nM–3 μM) on colon and rectum

Adult rats

In the adult rat colon, capsaicin (0.01 nM–3 μM) produced significantly higher contractions as compared to the vehicle control group ($P < 0.05$, two-way ANOVA, n = 4–6 [Figure 1a]). Each concentration of capsaicin produced a greater contractile response as compared to control ($P < 0.05$, Student's *t-test*, paired) except at the highest concentration that is, 3 μM. There is a sharp decline in contractile response at this concentration. Further, the increased contractile responses induced by capsaicin (0.01 nM–1 μM) were not dose dependent, and changes in contractile response at different concentrations from 0.01 nM to 1 μM were minimal and not significantly different. On application of 0.01 nM capsaicin, a sharp 31% increase in the contractile response was found, which was stable throughout the doses of 0.01 nM–1 μM.

A similar response was also observed in the adult rat rectum. However, at 3 μM concentration, the response of capsaicin abruptly declined (relaxation) and ended with significantly lower contractile tension as compared to vehicle control ($P<0.05$, two-way ANOVA, n = 4–6 [Figure 1b]).

Neonate rats

In contrast to the results of adult rats, the neonate rat colon, as well as rectum, failed to show any increase in contractile response to the application of capsaicin (0.01 nM–3 μM) as compared to vehicle control ($P > 0.05$, two-way ANOVA, $n = 6$ [Figures 2a and b]).

Effect of capsazepine (1 μM), a TRPV1 receptor blocker on colon and rectum of adult and neonate rats

The TRPV1 receptor blocker capsazepine (1 μM) failed to block the capsaicin-induced activity in the colon of an adult ($P > 0.05$, two-way ANOVA, $n = 6$ [Figure 3a]), but in a lower concentration, pre-treatment with capsazepine increased contractile tension in the adult rat rectum ($P < 0.05$, two-way ANOVA, $n = 6$ [Figure 3b]).

In the case of neonate rats, capsazepine (1 μM) had no effect on capsaicin-induced contractile activity in the colon as well as the rectum ($P > 0.05$, two-way ANOVA, n = 6 [Figure 4]).

Effect of L-NAME on colon and rectum of adult and neonate rats

Pre-treatment of the adult colon with L-NAME (100 μM) had no effect on the contractile activity of capsaicin in the adult colon ($P > 0.05$, two-way ANOVA, n = 6). In the case of the rectum, after pre-treatment with L-NAME, application of capsaicin increased contractile tension ($P < 0.05$, two-way ANOVA, $n = 6$ [Figure 5]).

In the case of neonate rats, L-NAME (100 μM) pre-treatment caused an increase in contractile tension in the colon of neonate rats ($P < 0.05$, two-way ANOVA, $n = 6$ [Figure 6a]). However, L-NAME (100 μM) had no effect on capsaicin activity in the rectum ($P > 0.05$, two-way ANOVA, $n = 6$ [Figure 6b]).

Effect of capsaicin (0.01 nM–3 μM) on contractile frequency (contractions/min) before and after pre-treatment with capsazepine (1 μM) and L-NAME (100 μM) in colon and rectum of adult and neonate rats

Capsaicin (0.01 nM–3 μM) increased contractile frequency significantly in both the colon and rectum of adult rats as compared to vehicle control. In the case of neonates, a significant decrease in contractile frequency was observed in the colon but no such response was observed in the neonate rectum.

When the colon and rectum of adult rats were pre-treated with capsazepine (1 μM) and L-NAME (100 μM), there was a further decrease in the contractile frequency as compared to the capsaicin-only treated group.

In the case of neonates, capsazepine pre-treatment also produced a similar change in frequency in both the colon and rectum as seen in adults. However, pre-application of

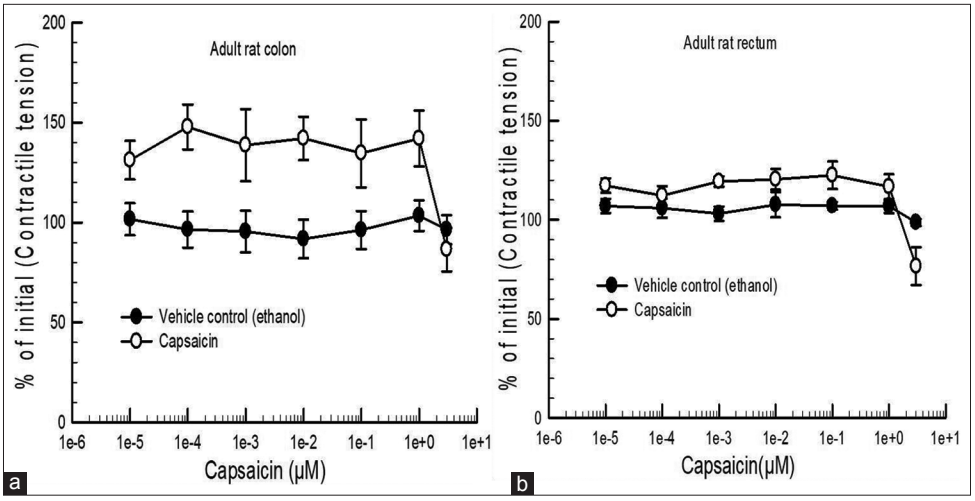

Figure 1: Dose-response curve showing the effect of capsaicin (0.01 nM–3 μM)-induced contractile tension (% of initial) in colon (a) and rectum (b) of adult rats as compared to vehicle control (ethanol v/v ratio). Capsaicin produces increase in contraction tension in colon and rectum of adults ($P < 0.05$, two-way ANOVA). Data points indicate mean ± standard error of the mean values ($n = 4–6$).

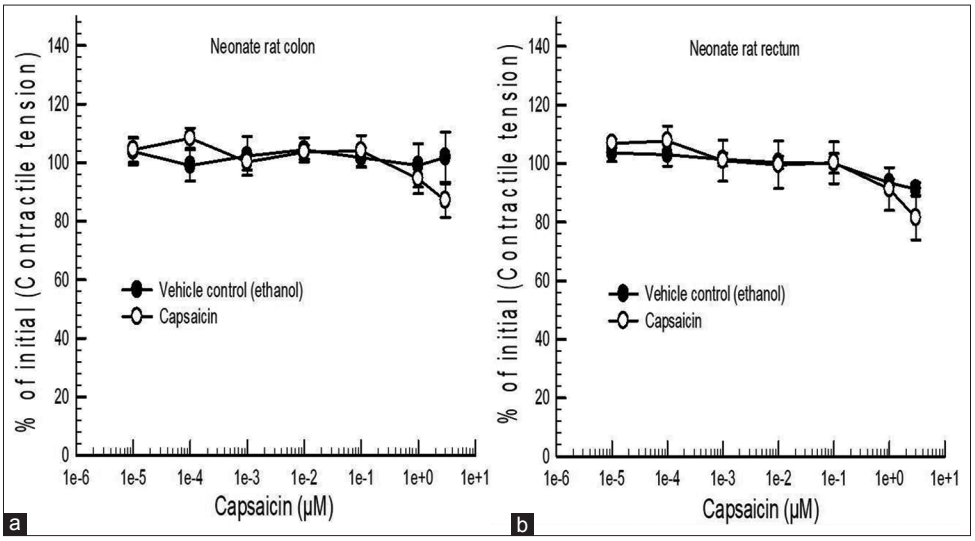

Figure 2: Dose-response curve showing the effect of capsaicin (0.01 nM–3 μM) on contractile tension (% of initial) in colon (a) and rectum (b) of neonate rats as compared to vehicle control (ethanol v/v ratio). Capsaicin failed to produce any change in contraction tension in colon and rectum of neonate rats ($P > 0.05$, two-way ANOVA). Data points indicate mean ± standard error of the mean values ($n = 6$).

L-NAME decreased frequency significantly in the neonate's colon but not in the rectum.

DISCUSSION

The present study was designed to determine the effect of capsaicin on the colon and rectum in neonatal rats and also to assess if the action of capsaicin is different in the neonate colon and rectum. In this study, it was observed that capsaicin raised contractile tension in the colon and rectum of adult rats, but no such response was observed in neonate rats [Figures 1 and 2]. However, capsaicin did affect the frequency of spontaneous contractions in the neonate's colon. Capsaicin-induced contractile responses have previously been observed in the adult guinea pig ileum, mouse jejunum, colon and rectum.[15,17,18,22] Similar responses are now being reported in the adult rat colon and rectum. A significant finding in this study is the failure of contractile response evoked by capsaicin in the neonate colon and rectum is a significant finding in this study. The non-responsiveness of the neonate colon or rectum may be due to the appearance of capsaicin receptors during a later stage of gut development.

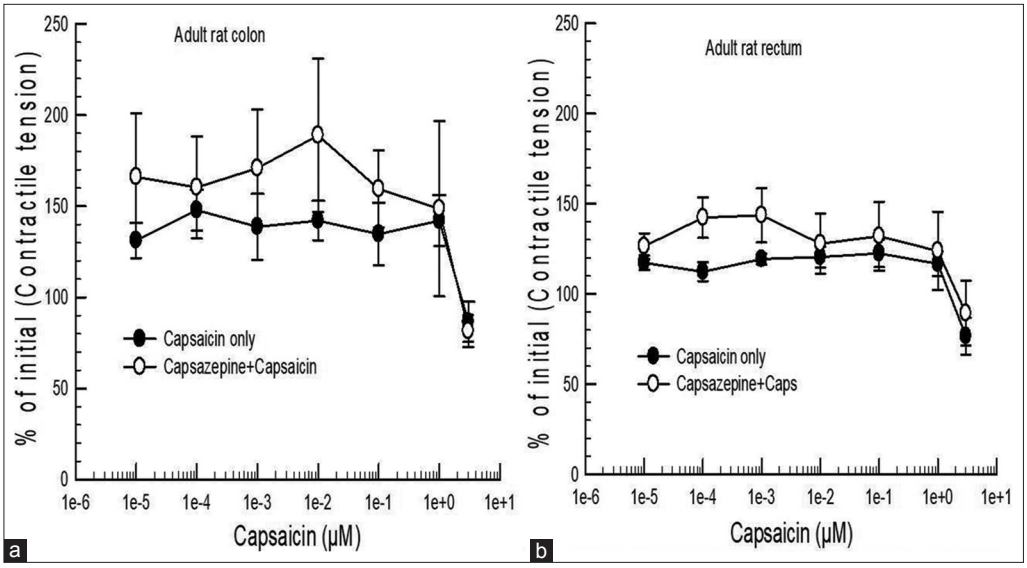

Figure 3: Dose-response curve showing the effect of capsaicin (0.01 nM–3 μM) on contractile tension (% of initial) in colon (a) and rectum (b) of adult rats after pre-treatment with capsazepine (1 μM). Capsaicin failed to produce any change in contraction tension in colon ($P > 0.05$, two-way ANOVA) but an increase in contractile tension in rectum ($P < 0.05$, two-way ANOVA). Data points indicate mean ± standard error of the mean values ($n = 6$).

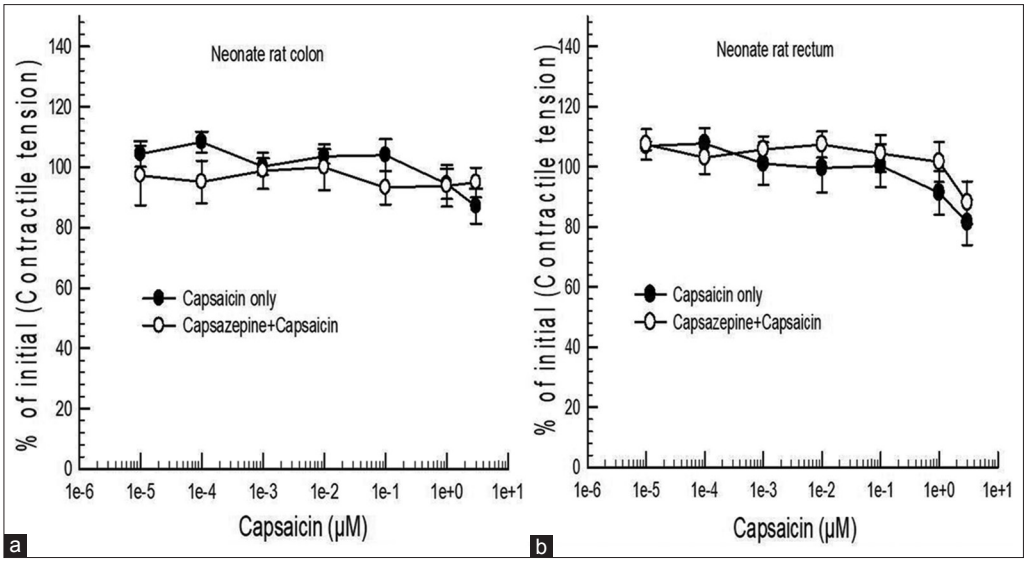

Figure 4: Dose-response curve showing the effect of capsaicin (0.01 nM–3 μM) on contractile tension (% of initial) in colon (a) and rectum (b) of neonate rats after pre-treatment with capsazepine (1 μM). Capsaicin failed to produce any change in contractile tension in colon and rectum after pre-treatment with capsazepine ($P > 0.05$, two-way ANOVA). Data points indicate mean ± standard error of the mean values ($n = 6$).

Capsaicin has been observed to mediate its action through TRPV1 and NO in intestinal smooth muscle in various species.[15,19,22] In rats, in the present study, TRPV1 receptor antagonist capsazepine (1 μM) not only failed to block the capsaicin-induced response, but it enhanced the capsaicin-evoked contractile response in the adult rat rectum [Figure 3]. At present, it is difficult to explain how capsazepine could potentiate the tone in the rectum while sparing the colon. Nevertheless, it indicated a difference between the rectum and the colon in terms of the mechanism of action of capsaicin. This response of capsazepine in the rat is different from those reported in the mouse small intestine, in which capsazepine blocked the capsaicin-induced contractions.[22] In another study on the mouse large intestine, it was reported that

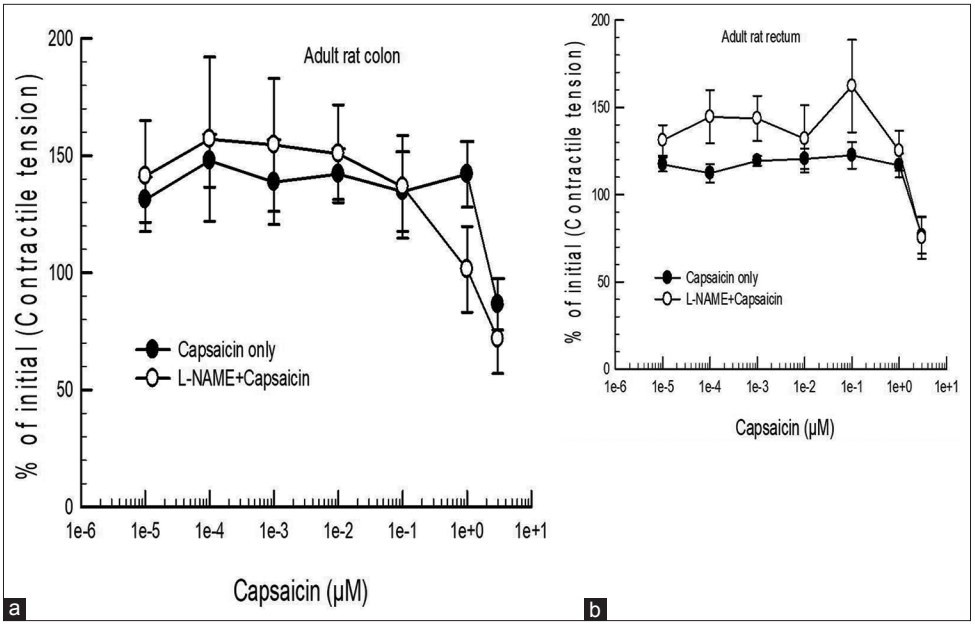

Figure 5: Dose-response curve showing the effect of capsaicin (0.01 nM–3 μM) on contractile tension (% of initial) in colon (a) and rectum (b) of adult rats after pretreatment with L-NAME (100 μM). Capsaicin failed to produce any change in contraction tension in colon ($P > 0.05$, two-way ANOVA) but causes an increase in contractile tension in rectum ($P < 0.05$, two-way ANOVA). Data points indicate mean ± standard error of the mean values ($n = 6$).

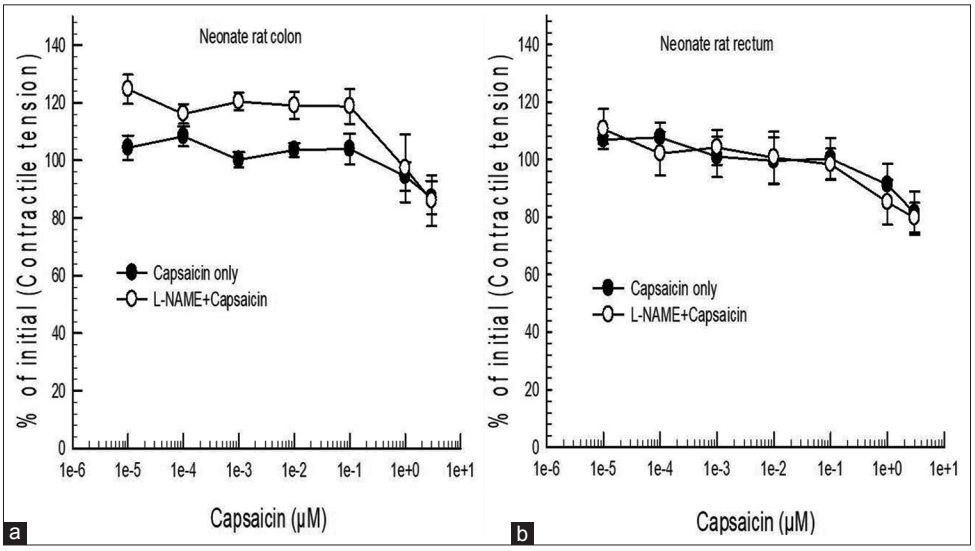

Figure 6: Dose-response curve showing the effect of capsaicin (0.01 nM–3 μM) on contractile tension (% of initial) in colon (a) and rectum (b) of neonate rats after pretreatment with L-NAME (100 μM). Capsaicin causes an increase in contractile tension in colon ($P < 0.05$, two-way ANOVA) but not in rectum after pre-treatment with L-NAME ($P > 0.05$, two-way ANOVA). Data points indicate mean ± standard error of the mean values ($n = 6$).

lower concentrations of TRPV1 antagonists such as BCTC and iodoresiniferatoxin are ineffective in the prevention of contractions induced by capsaicin.[15] It may be interesting to note that, in the case of the neonate rat, capsazepine failed to affect the capsaicin-induced contractile tension in both colon and rectum [Figure 4], suggesting non-involvement of TRPV1 receptors in the neonate.

Further, pre-application of L-NAME (100 μM), a nitric oxide synthase inhibitor, potentiated capsaicin-induced

response in the adult rectum and neonate's colon but had no effect in the neonate rectum and adult colon [Figures 5 and 6]. Increased contractile tension that appeared in the neonate rat colon and adult rectum after pre-treatment with L-NAME may be due to inhibition of natural NO present and may have acted independent of capsaicin. This type of NO activity is not observed when the colon matures to an adult level. Natural NO activity, on the other hand, is likely to be at its lowest in the neonate rectum before reaching adulthood. An earlier study in the mouse large intestine also showed that L-NAME was ineffective in mediating capsaicin-induced contractile response as observed in the present study in the adult colon.[16]

In the present investigation, the analysis of contractile frequency records showed that capsaicin with a low concentration (0.01 nM–0.01 μM) increased contractile frequency in both the colon and rectum of adult rats as compared to vehicle control. However, the dose-response curve showed that the effect of capsaicin on frequency was abolished at higher concentrations (0.01 μM–3 μM). In earlier studies, it was reported that capsaicin with a high concentration caused a decrease in contractile frequency in the cat colon and mouse small intestine.[28,29] The difference in the response may be attributed to the very high concentration (50–100 μM) of capsaicin used by these workers. Thus, it may be assumed that capsaicin increases the frequency at low concentrations and depresses the frequency at high concentrations. This might be attributed to the desensitisation of the receptors at high concentrations.

In the present experiment, capsaicin-evoked changes in contractile frequency in adult rats were blocked by capsazepine and L-NAME. These indicated that the action of capsaicin was mediated through the TRPV1 receptor and NO in adult rats. A study on the pacemaker activity of interstitial cells of Cajal from the mouse small intestine could not detect the involvement of TRPV1 or NO.[29] Hence, it is possible that frequency may be controlled by a path that does not involve TRPV1 or NO.

In contrast to adults, capsaicin at the lower concentration (0.01 nM–0.01 μM) did not show any change in frequency in the neonatal colon, while a decrease in contractile frequency was observed with a higher concentration (0.1 μM–3 μM) of capsaicin. In the case of neonates, capsazepine pre-treatment also produced changes in frequency for both colon and rectum, similar to what was seen in adults. However, pre-application of L-NAME decreased frequency in the neonate rectum but not in the colon. Therefore, it appeared that the signalling pathway for frequency regulation in the neonate rectum was different from that in the colon because the frequency of colonic contractions could be regulated independent of NO production in neonates.

Antagonism between capsaicin and capsazepine occurs on interaction not only with TRPV1 channels but also with neuromimetic membranes, as was recently discovered in a study that concluded that capsaicin and capsazepine interact with lipid bilayers made up of phospholipids and cholesterol to change the membrane fluidity of those lipid bilayers in different ways.[30]

CONCLUSION

It may be concluded that the absence of capsaicin-induced contractile tension in the neonate colon and rectum could be due to the late appearance of capsaicin receptors during the postnatal gut development process. Capsaicin-induced changes in contractile activity may or may not involve TRPV1 or the NO pathway, depending on the part of the large gut (colon or rectum) and developmental maturity (neonate or adult).

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Batiha GE, Alqahtani A, Ojo OA, Shaheen HM, Wasef L, Elzeiny M, *et al*. Biological properties, bioactive constituents, and pharmacokinetics of some *Capsicum* spp. and Capsaicinoids. Int J Mol Sci 2020;21:5179.
2. Barthó L, Benkó R, Patacchini R, Pethö G, Holzer-Petsche U, Holzer P, *et al*. Effects of capsaicin on visceral smooth muscle: A valuable tool for sensory neurotransmitter identification. Eur J Pharmacol 2004;500:143-57.
3. Schmidt B, Hammer J, Holzer P, Hammer HF. Chemical nociception in the jejunum induced by capsaicin. Gut 2004;53:1109-16.
4. Laird JM, Martinez-Caro L, Garcia-Nicas E, Cervero F. A new model of visceral pain and referred hyperalgesia in the mouse. Pain 2001;92:335-42.
5. Gonzalez R, Dunkel R, Koletzko B, Schusdziarra V, Allescher HD. Effect of capsaicin-containing red pepper sauce suspension on upper gastrointestinal motility in healthy volunteers. Dig Dis Sci 1998;43:1165-71.
6. Debreceni A, Abdel-Salam OM, Figler M, Juricskay I, Szolcsányi J, Mózsik G. Capsaicin increases gastric emptying rate in healthy human subjects measured by 13C-labeled octanoic acid breath test. J Physiol Paris 1999;93:455-60.

7. Chan CL, Facer P, Davis JB, Smith GD, Egerton J, Bountra C, *et al*. Sensory fibres expressing capsaicin receptor TRPV1 in patients with rectal hypersensitivity and faecal urgency. Lancet 2003;361:385-91.
8. Akbar A, Yiangou Y, Facer P, Walters JR, Anand P, Ghosh S. Increased capsaicin receptor TRPV1-expressing sensory fibres in irritable bowel syndrome and their correlation with abdominal pain. Gut 2008;57:923-9.
9. Akbar A, Yiangou Y, Facer P, Brydon WG, Walters JR, Anand P, *et al*. Expression of the TRPV1 receptor differs in quiescent inflammatory bowel disease with or without abdominal pain. Gut 2010;59:767-74.
10. Caterina MJ, Schumacher MA, Tominaga M, Rosen TA, Levine JD, Julius D. The capsaicin receptor: A heat-activated ion channel in the pain pathway. Nature 1997;389:816-24.
11. Zhang L, Lu W, Lu C, Guo Y, Chen J, Xu F, *et al*. Beneficial effect of capsaicin via TRPV4/EDH signals on mesenteric arterioles of normal and colitis mice. J Adv Res 2022;39:291-303.
12. Jones RC 3rd, Xu L, Gebhart GF. The mechanosensitivity of mouse colon afferent fibers and their sensitization by inflammatory mediators require transient receptor potential vanilloid 1 and acid-sensing ion channel 3. J Neurosci 2005;23:10981-9.
13. Seebohm G, Schreiber JA. Beyond hot and spicy: TRPV channels and their pharmacological modulation. Cell Physiol Biochem 2021;55:108-30.
14. Yu X, Yu M, Liu Y, Yu S. TRP channel functions in the gastrointestinal tract. Semin Immunopathol 2016;38:385-96.
15. Matsumoto K, Hosoya T, Tashima K, Namiki T, Murayama T, Horiea S. Distribution of transient receptor potential vanilloid 1 channel-expressing nerve fibers in mouse rectal and colonic enteric nervous system: Relationship to peptidergic and nitrergic neurons. Neuroscience 2011;172:518-34.
16. Matsumoto KE, Kurosawa E, Terui H, Hosoya T, Tashima K, Murayama T, *et al*. Localization of TRPV1 and contractile effect of capsaicin in mouse large intestine: High abundance and sensitivity in rectum and distal colon. Am J Physiol Gastrointest Liver Physiol 2009;297:348-60.
17. Bartho´ L, Szolcsanyi J. The site of action of capsaicin on the guinea-pig isolated ileum. Naunynschmiedebergs Arch Pharmacol 1978;305:75-81.
18. Bartho´ L, Benko´ R, Lazar ZS, Illenyi L, Horvath OP. Nitric oxide is involved in the relaxant effect of capsaicin in the human sigmoid colon circular muscle. Naunynschmiedebergs Arch Pharmacol 2002;366:496-500.
19. Benko R, Lazar Z, Undi S, Illenyi L, Antal A, Horvath OP, *et al*. Inhibition of nitric oxide synthesis blocks the inhibitory response to capsaicin in intestinal circular muscle preparations from different species. Life Sci 2005;76:2773-82.
20. Toh CC, Lee TS, Kiang AK. The pharmacological actions of capsaicin and analogues. British J Pharmacol 1955;10:175-82.
21. Chahl LA. Evidence that the contractile response of the guinea-pig ileum to capsaicin is due to substance P release. Naunynschmiedebergs Arch Pharmacol 1982;319:212-5.
22. DE Man JG, Boeckx S, Anguille S, Winter BY, Schepper HU, Herman AG, *et al*. Functional study on TRPV1-mediated signalling in the mouse small intestine: involvement of tachykinins receptors. Neurogastroenterol Motil 2008;20:546-56.
23. Perna E, Aguilera-Lizarraga J, Florens MV, Jain P, Theofanous SA, Hanning N, *et al*. Effect of resolvins on sensitisation of TRPV1 and visceral hypersensitivity in IBS. Gut 2021;70:1275-86.
24. Rofes L, Arreola V, Martin A, Clavé P. Natural capsaicinoids improve swallow response in older patients with oropharyngeal dysphagia. Gut 2013;62:1280-7.
25. Allescher HD, Sattler D, Piller C, Schusdziarra V, Classen M. Ascending neural pathways in the rat ileum in *in vitro*-effect of capsaicin and involvement of nitric oxide. Eur J Pharmacol 1992;217:153-62.
26. Tyagi P, Mandal MB, Mandal S, Patne SC, Gangopadhyay AN. Pouch colon associated with anorectal malformations fails to show spontaneous contractions but responds to acetylcholine and histamine *in vitro*. J Pediatr Surg 2009;44:2156-2.
27. Singh S, Mandal MB. *In vitro* study of acetylcholine and histamine induced contractions in colon and rectum of adult and neonate rats. Indian J Physiol Pharmacol 20132;57:104.
28. Anuras S, Christensen J, Templeman D. Effect of capsaicin on electrical slow waves in the isolated cat colon. Gut 1977;18:666-9.
29. Choi S, Sun JM, Shahi PK, Zuo DC, Kim H, Jun JY. Capsaicin inhibits the spontaneous pacemaker activity in interstitial cells of cajal from the small intestine of mouse. J Neurogastroenterol Motil 2010;16:265-73.
30. Mizogami M, Tsuchiya, H. Membrane interactivity of capsaicin antagonized by capsazepine. Int J Mol Sci 2022;23:3971.

How to cite this article: Singh S, Sharma P, Dixit D, Mandal MB. Capsaicin fails to produce changes in contractile tension in large gut of neonate rats. Indian J Physiol Pharmacol 2023;67:36-43.