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Ionic Channel Blockage Effect on the Electromechanical Model of Human Gastric Wall Smooth Muscle Cells

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In this paper, a three-dimensional electromechanical model is presented to investigate the effect of calcium and potassium ionic channels on the contractile behavior of human gastric wall smooth muscle cells with the finite element approach. In this model, simultaneous electrical and mechanical interactions of 240-cells and 548-links were considered. Electrophysiological interactions of cells through ion channels with the extrascellular environment and gap junctions with adjacent cells lead to the production and propagation of slow waves in smooth muscle. This wave causes contraction and peristaltic movements in the muscles of the gastric wall. By blocking calcium and potassium ionic channels by pharmacological agents can be improved disorders caused by these movements and contractions and brought them closer to the physiological state.

Keywords: Electromechanical model, Smooth muscle cell, Gastric, Ion Channel Blocker, Contraction.

1 Introduction

The distribution of the electromechanical stimulation wave in response to electrophysiological stimulation causes smooth muscle contraction and peristaltic motilities in the gastric. The generation and propagation of peristaltic movements of the stomach play an essential role in grinding food, mixing the secretion of enzymes and stomach acid with food, and Propulsion its contents to the intestine [1, 2]. The action potential is created by the electrophysiological interaction of cells with the extracellular environment through ion channels in the cell membrane [3] and is propagated to the adjacent cells through gap junctions and spreads

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throughout the gastric wall [4]. The action potential in smooth muscle is interpreted as a slow wave. This study aimed to investigate the effects of calcium and potassium ion channels in the electromechanical model and the rate of contraction in the human gastric wall smooth muscle (HGWSM) cells.

So far, theoretical and computational studies related to soft tissue contraction have mainly dealt with the behavior of skeletal muscles [5, 6] and the heart [7, 8]. Also, Electrophysiological, electrochemical, and stimulation wave propagation models are presented in the heart tissue [9, 10]. However, less attention has been paid to modeling the motility and function of the gastrointestinal tract, which is due to its structural and functional complexity [2, 11]. So far, limited research has been done on the mechanism of gastrointestinal contractions relative to the heart [12].

In previous research, certain parts have been studied of the mechanical behavior of the gastrointestinal tract. Colon strain during colonoscopy and diverticulosis stress in the colon has been simulated [13, 14]. A cylindrical model has been proposed to study gastric motility considering smooth muscles [15]. A three-dimensional cylindrical model of esophageal peristaltic behavior with its layers is presented based on elastic and isotropic models [16]. According to Gasser-Ogden-Holzapfel's theory and based on elastic properties, a model of the intestine is presented [17]. In these models, the structure of the organs of the gastrointestinal tract is designed as a tube, then layers and properties are assigned to this tubular structure. Finally, the resulting stress and strain are investigated. In addition, studies have been performed to describe gastric fluid flow based on artificial deformation in the gastric geometry model and the investigation of internal flows [18-20]. These models have been done considering the mechanical properties of the organs, but have not considered electrophysiological and electromechanical properties and their interaction with each other.

In this paper, the effect of calcium and potassium ion channel blockage was investigated on the electromechanical model of human gastric smooth muscle cells. The electromechanical model presented in this study is based on the electrophysiological details of the cell, the interaction of cells and muscles with each other, the distribution and propagation of the excitation wave in the tissue, the function, and characteristics of ion channels, which are very different from previous research. In the simulation of this model, simultaneous electrical and mechanical interactions are considered. The mechanical approach includes modeling muscle by elastic and contractile components. Additionally, the electrophysiological approach includes modeling ionic interactions of each cell with the extracellular environment and adjacent cells [21]. So that it is possible to study the pharmacological and pathological effects on the behavior of each ion channel on the mechanical performance of the model. Using this model can be observed tissue contraction due to inhibition of ion channels in the cellular-muscular model. Also, motility and contraction disorders in the smooth muscle of the gastrointestinal tract can be improved by using pharmacological agents, ion channel blockers, and the bioelectronic implants [22].

2 Materials and Method

2. 1 Slow wave generation and distribution in HGWSM

Cells are performed electrochemical interaction with the extracellular environment and interstitial fluid through the excitable membrane and with neighboring cells via gap junctions [4]. Ion interaction between intracellular and extracellular environments takes place through ion channels in the cell membrane. From the sum currents passing through the cell membrane, the total current of the cell is formed. The total current of the cell also depends on the stimulation current produced by the Interstitial Cells of Cajal in the smooth muscle. The total current of the cell (I_{ion}) is given in Eq. (1).

$$I_{ion} = I_K + I_{Na} + I_{Ca} + I_{Lekages} + I_{Exchangers} + I_{Pumps} + I_{Stimulation} \quad (1)$$

Where I_K is the potassium currents, I_{Na} is the sodium current, I_{Ca} calcium currents, I_{Lekage} is the background leakage currents, $I_{Exchangers}$ is the exchanger currents such as sodium-calcium exchanger, I_{Pumps} is the pomp currents such as sodium–potassium pump, and $I_{Stimulation}$ is the stimulus current. All currents are in pA.

These interactions and transfers of the ions cause changes in the membrane potential difference and ultimately lead to the generation of action potentials [3]. The change in cell membrane voltage occurs based on the Hodgkin-Huxley differential equation. In their research, the cell membrane is assumed to be an electronic circuit. In this equation, changes in cell membrane potential depend on the total current passing through the cell membrane and the capacitance of the cell [23].

$$\frac{\delta V_m}{\delta t} = -\frac{I_{ion}}{C_m} \tag{2}$$

Where I_{ion} is the total current of the cell in pA, C_m is the cell capacitance in pF, V_m is the membrane potential in mV and t is the time in ms. This formula shows the changes in cell membrane voltage due to the transfer of ions between the intracellular and extracellular environments via ion channels. To consider ion interactions between adjacent cells through gap junctions, Eq. (2) can be generalized as a differential Eq. (3). In this formula, parameter ∇(D∇V) shows the potential changes of cell membranes in ionic interactions with neighboring cells [24].

$$\frac{\delta V}{\delta t} = \frac{f(V,u)}{C_m} + \nabla(D\nabla V) \tag{3}$$

In Eq. (3), $f(V,u)$ is the simultaneous effect of membrane voltage, ionic current parameters, and ion channel gates coefficients, C_m is the cell capacitance and $\nabla(D\nabla V)$ is related to gap junctions and indicates the volumetric distribution of the electrical potential of cell assemblies in the tissue. Parameter $\nabla(D\nabla V)$ is described as Eq. (4).

$$\nabla(D\nabla V) = D\nabla^2 V = D(\frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2})V \tag{4}$$

Where D is the spatial function of voltage propagation, ∇^2 is the Laplacian Operator and V is the membrane potential. The Laplace operator represents the potential distribution of the membrane in the tissue in three directions *x*, *y*, and *z*. The D function can also be considered isotropic and homogeneous [25].

The production and propagation of slow waves in smooth muscle cells depend on the total current of the cell. The total current of the cell is created by the sum of currents of which include calcium and potassium currents. To investigate the effect of calcium and potassium channels on slow wave distribution, those channels were blocked. These blockages were applied in two states: 50% and 100% in the channels. To simulate channel blockade, the maximum channel conductance parameter was considered [26]. The general formula describes each current as Eq. (5). In the smooth muscle cell of the gastrointestinal tract, there are usually two types of calcium channels (L-type and T-type) and two types of potassium channels (potassium and fast potassium) [26-28]. For example, this equation relates to the current of the L-type calcium channel.

$$\mathrm{I_{Ca-L}} = \mathrm{G_{Ca-L}} * \mathrm{d_{Ca-L}} * \mathrm{f_{Ca-L}} * (\mathrm{V_m} - \mathrm{E_{Ca}}) \tag{5}$$

In Eq. (5), I_{Ca-L} is the general current of the L-type calcium channel, G_{Ca-L} is the maximum conductance of the channel, d_{Ca-L} is the activation gating variable, f_{Ca-L} is the inactivation gating variable, V_m is the membrane potential and E_{Ca} is the Nernst potential for the calcium ion. It should be noted that in the general current formula, other currents also have corresponded parameters. After blocking the calcium and potassium channels, which causes changes in the slow wave compared to the physiological state, the distribution of this wave on the electromechanical model is investigated.

2. 2 The HGWSM electromechanical model

The geometric arrangement of the cell layers on top of each other was used to simulate the electromechanical model of HGWSM tissue (cellular-muscular model). The cellular-muscular model of HGWSM tissue is shown in Figure (1).
The model intended for HGWSM tissue includes 240 nodes (cells) and 548 links (muscles). These cells are arranged in 6 rows, 20 columns, and 2 floors next to each other to model the electromechanical behavior of a layer of longitudinal muscle in the gastric wall.
In this model, each cell was considered as a node. There are links between nodes that simulated the function of gastric smooth muscle fibers. The simultaneous effect of active contraction and passive deformation was considered for the links. The production and distribution of electrical stimulation cause contraction in the electromechanical model. The propagation of electrical stimulation causes the mechanical contraction in the model and the electromechanical wave is propagated throughout the model due to the elasticity of the links.
A simplified Hill model was considered to illustrate the electromechanical function of smooth muscle fibers in HGWSM tissue. A simplified model of Hill is shown in Figure (2). This model is made up of two parts, contractile and elastic, in the series. In this model, the contractile component simulates active muscle function, and the elastic component simulates passive muscle function.

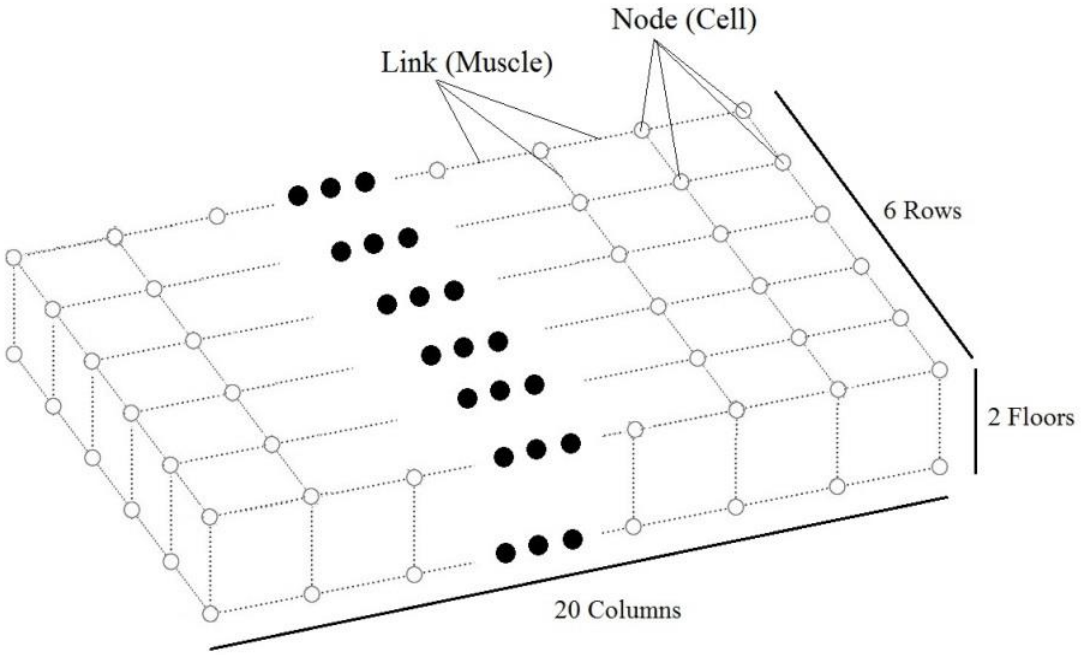

Figure 1 Electromechanical model of HGWSM (cellular-muscular model), including 240 nodes (cells) and 548 links (muscle). These cells are arranged in 6 rows, 20 columns, and 2 floors.

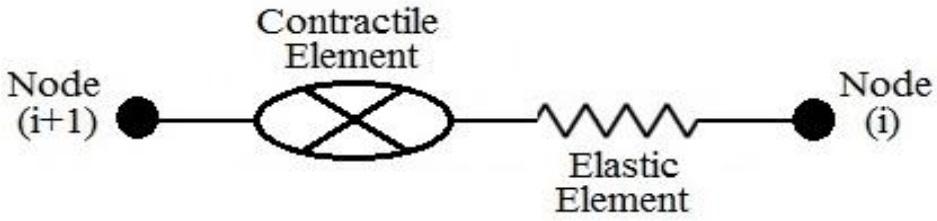

Figure 2 Hill simplified model. This model is located between two consecutive nodes ($Node_i$ and $Node_{i+1}$). This model also includes contractile and elastic components that are placed next to each other in series.

The change in muscle length (δ_{Muscle}) according to Eq. (6) is equal to the sum of the changes in the length of both the elastic ($\delta_{Elastic}$) and contractile ($\delta_{Contractile}$) components in the simplified Hill model.

$$\delta_{Muscle} = \delta_{Elastic} + \delta_{Contractile} \quad (6)$$

The HGWSM model was created by connecting links and nodes to each other and simulating the electromechanical behavior of the model using the finite element approach. Then, the above model is added to all the muscle fibers (links) of the HGWSM structure. Finally, the electromechanical performance can be deduced from the interaction of the electrophysiological and electrochemical behaviors of the HGWSM model. The function of the muscle model in HGWSM tissue is based on electrophysiological details in the ion channels of the excitable membrane of gastric muscle cells and the propagation of slow waves across the gastric wall. This electrical stimulation causes the mechanical contraction in the force-producing component of the muscle fibers. The contractile force produced wants to shorten the length of the muscle fiber, but the attachment of the muscle fiber from its end to the other muscle fibers opposes this contraction. This discrepancy causes an interactive deformation in the cellular-muscular model, the production of peristaltic movements, and contraction in the model. Finally, deformation occurs in the electromechanical HGWSM model. This deformation is due to the simultaneous interaction between fibers and cells in the model. The Spatio-temporal distribution of the electrical potential of the gastric wall has been considered from Corrias and Buist's research as a stimulus function in the model [27].

Corrias and Buist's model was used to simulate the electrophysiological behavior of gastric cells [27] and Tabatabai et al. model was used to simulate the electromechanical behavior of cells and muscles based on analogy and thermomechanical interactions [9, 10]. Then, the slow wave distribution was applied on the electromechanical model of HGWSM in physiological state, 50% and 100% blockage in L-type and T-type calcium channels, potassium, and fast potassium channels. Finally, the deformation of the HGWSM electromechanical model in the ionic channel blockage state was compared with the physiological state.

2. 3 The Numerical simulation

The main purpose of this study was to investigate the effect of electrophysiological wave distribution of gastric wall cells on the contraction of the electromechanical cellular-muscular model. The finite element method has been used to model and simulate this structure. This simulation was performed in ANSYS 14 software and ANSYS Parametric Design Language (APDL) environment. The cellular-muscular model was written and executed by macro code in the APDL environment of ANSYS software. The total number of nodes considered in this model is equal to 240 nodes, which are written by nested loops using macro coding in three directions X, Y, Z. The coordinates of the nodes are considered in Eq. (7).

$$\mathrm{Node_m} = [\,\mathrm{i} \quad \mathrm{j} \quad \mathrm{k}\,] \tag{7}$$

In Eq. (7), the parameter i is in the direction of the x-axis, the parameter j is in the direction of the y-axis, and the parameter k is in the direction of the z-axis, which their numbers increased from 1 to 6, 1 to 2, and 1 to 20, respectively. The nodes were connected by 548 links. Each link connects the node ($\mathrm{Node_m}$) to the next node ($\mathrm{Node_{m+1}}$). The links were defined by nested loops in macro code and formed the line body model with the nodes. The links are of the Link-180 type. this element type is the uniaxial compression-tension element. Each link was considered as an element and their meshing was assumed to be a line such as the truss members. The properties of all elements were assumed to be the same (such as the cross-section of element (A), the modulus of elasticity (E), the Poisson's ratio (ν), and the coefficient of thermal expansion (α)). The element matrix is shown in Eq. (8).

$$\mathrm{Element_n} = [\,\mathrm{Node_m} \quad \mathrm{Node_{m+1}} \quad \mathrm{A} \quad \mathrm{E} \quad \nu \quad \alpha\,] \tag{8}$$

Support in some nodes was considered by Eq. (9). In this equation, the pin support with the symbol 0 and the roller support with the symbol 1 were considered for the $\mathrm{support_{type}}$ parameter. Also, the movement constraints were considered in the x-direction with the symbol 0, in the y-direction with the symbol 1, in the z-direction with the symbol 2, and all directions with the symbol 3 for the $\mathrm{support_{orientation}}$ parameter.

$$\mathrm{Support} = [\,\mathrm{Node_m} \quad \mathrm{support_{type}} \quad \mathrm{support_{orientation}}\,] \tag{9}$$

The analogy approach was used to apply voltage to the nodes. First, the membrane potential was obtained from the slow wave simulation of gastric cells in the electrophysiological stage. Then, the voltage obtained from the electrophysiological simulation with macro code was applied to the nodes of the electromechanical model as a function of temperature. The voltage matrix applied to each node is given in Eq. (10).

$$\mathrm{V} = [\,\mathrm{Node_m} \quad \mathrm{V_m}\,] \tag{10}$$

Finally, the total stiffness matrix (K) was formed by considering the stiffness matrix of each element, and the equation of displacement of nodes (u) was solved in the model (Eq. 5).

$$[\mathrm{K}] * \{\mathrm{u}\} = \{\mathrm{V}\} \tag{11}$$

From macro code was used to model all states in HGWSM [physiological state, half and full blockage of two calcium channels (type L and T) and two potassium channels]. And the highest contraction was compared between all states. The reason for using macro code in the APDL environment was to simplify the model, have a large number of outputs, increase the speed of program execution, and reduce the processing time.

3 Results

3.1 Contraction of HGWSM electromechanical model in physiological state

The smooth muscles of the gastric wall need electrical stimulation to create contractions and peristaltic motilities. Electrical stimulation of the stomach is caused by the production and propagation of slow waves in the gastric smooth muscle cells and distribution to the entire

tissue. The model presented in this paper is the cellular-muscular model. This model has the ability to excitability and flexibility simultaneously. The deformation of this model was considered as the contraction of HGWSM tissue in several parts of the stomach wall of the physiological state.
In the HGWSM electromechanical model, cells and links are connected in three dimensions. So that if they are subjected to electrophysiological stimulation, the length of the links will change and cause a mechanical deformation in the model. Finally, the links come together to create a new electromechanical balance.
The contraction simulation results of the electromechanical model of HGWSM tissue under physiological conditions are shown in Figure (3a) to Figure (3d). Figure (3) shows the contractions of the longitudinal muscle layer of the gastric body in four parts as follows. The initial contraction at the beginning of the gastric body (Figure 3a), Expansion of slow wave and muscle contracted at the upper part of the greater curvature of the gastric (Figure 3b), muscle contraction due to slow-wave propagation at the lower part of the greater curvature of the gastric (Figure 3c), and final contraction at the end of the gastric body (Figure 3d).
Electrical stimulation begins at the border between the fundus and the stomach body. This stimulation creates a slow wave and causes an initial contraction in this region [15]. Figure (3a) shows the areas around the beginning of the body of the gastric contracted, and this contraction is also shown as an indent in the HGWSM model. As shown in Figures (3b) and (3c), a slow wave propagates over time in the model and gradually reaches the middle parts of the stomach body, and causing these areas to contract. Finally, Figure (3d) shows the contraction of the model at the end of the gastric wall. A slow wave through any area at the gastric wall passes, then the region is contracted. After passing the slow wave, that area returns to its previous shape. This contraction process continues from the beginning of the gastric body to the antrum and pylorus, and the contents of the gastric are Evacuated into the duodenum (Figures 3a to 3d). This operation begins with automatic stimulation at the beginning of the gastric body and is repeated at the frequency of about 2.81 cycles per minute [27, 29].

3.2 Contraction of HGWSM electromechanical model in blockage of L-type and T-type calcium channels

Channel inhibition was performed in two states of half and full block to investigate the effect of blockage of L-type and T-type calcium channels on the contraction of the electromechanical model of HGWSM tissue. Then, the effect of electrophysiological stimulation wave distribution on four selected parts in the gastric wall was investigated (the beginning of the gastric body, the upper part of the greater curvature of the gastric, the lower part of the greater curvature of the gastric, the end of the gastric body). The results of contraction are expressed as a percentage in comparison with the physiological state.
Contraction of the electromechanical model of HGWSM tissue on L-type and T-type calcium channels is reduced by applying half and full channel blockage in all four parts of the gastric. The results of the L-type calcium channel blockade are given in Table (1) and the results of the T-type calcium channel blockade are given in Table (2).
According to the results of Table (1), it is clear that the contraction in the state of complete channel blockage is less than the 50% blockage and less than the physiological state. The results of Table (2) show that the contraction in the full channel blockage is less than 50% channel blockage and less than in the physiological state. From the results of Tables (1) and (2), it can be concluded that inhibition of calcium channels reduces the contraction of the HGWSM tissue model compared to the physiological state. Also, The results showed that the effect of the L-type calcium channel blockade in reducing HGWSM tissue contraction is greater than the T-type calcium channel.

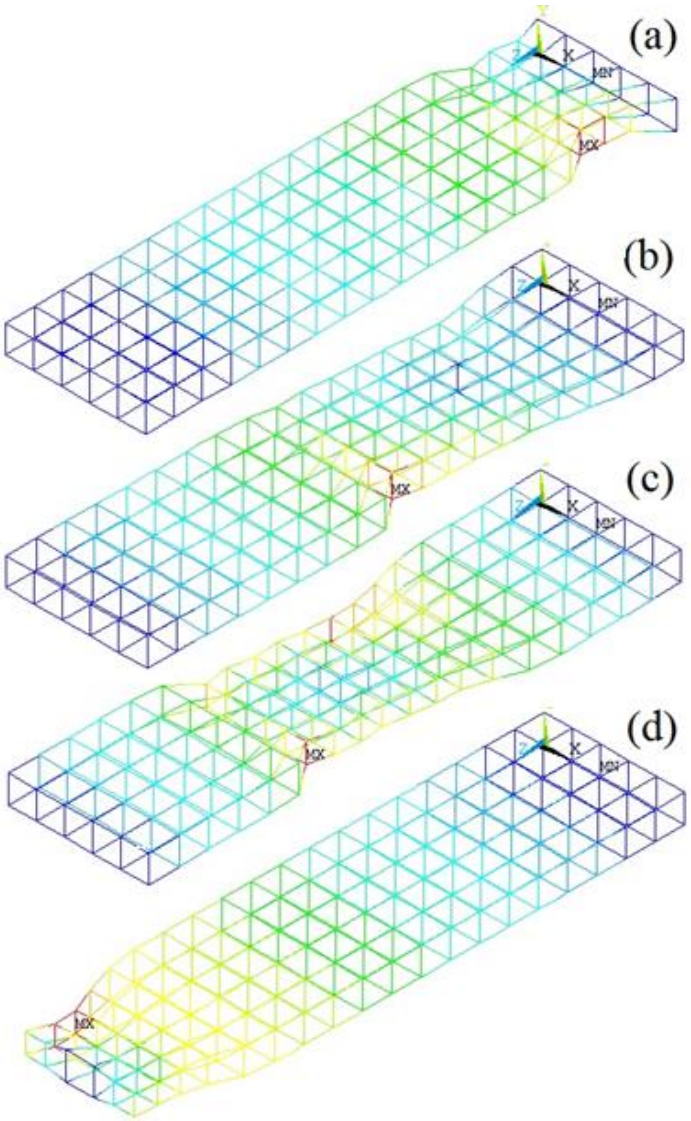

Figure 3 Electromechanical contraction of the HGWSM tissue model in physiological state. a) The beginning of the gastric body, b) The upper part of the greater curvature of the gastric, c) The lower part of the greater curvature of the gastric, d) The end of the gastric body.

Table 1 Percentage of maximal contraction of the electromechanical model of HGWSM tissue in four parts of the gastric body, under two states of L-type calcium channel blockade (half and full) compared to the physiological state.

Part	50% blocked	100% blocked
the beginning of the gastric body	-1.80 %	-3.72 %
the upper part of the greater curvature of the gastric	-1.81 %	-3.72 %
the lower part of the greater curvature of the gastric	-1.81 %	-3.72 %
the end of the gastric body	-0.14 %	-0.27 %

* (Negative sign means less contraction than physiological state)

Table 2 Percentage of maximal contraction of the electromechanical model of HGWSM tissue in four parts of the gastric body, under two states of T-type calcium channel blockade (half and full) compared to the physiological state.

Part	50% blocked	100% blocked
the beginning of the gastric body	-1.03 %	-1.97 %
the upper part of the greater curvature of the gastric	-1.03 %	-1.97 %
the lower part of the greater curvature of the gastric	-1.03 %	-1.97 %
the end of the gastric body	-0.54 %	-1.07 %

* (Negative sign means less contraction than physiological state)

3.3 Contraction of HGWSM electromechanical model in blockage of potassium and fast potassium channels

To investigate the effect of potassium and fast potassium channel inhibition on the contraction of the HGWSM electromechanical tissue model, channel blockade was performed in 50% and 100% states. The results were expressed as a percentage in comparison with the contraction of the physiological state in different parts of the gastric wall. Selected parts of the gastric wall are as follows: the beginning of the gastric body, the upper part of the greater curvature of the gastric, the lower part of the greater curvature of the gastric, the end of the gastric body.
By applying 50% and 100% blockage to potassium and fast potassium channels in all four parts, the contraction in the electromechanical model of HGWSM tissue increases. The results are given for potassium and fast potassium channels in Tables (3) and (4), respectively.
The results of Table (3) show that the contraction in the state of complete blockage of the potassium channel is greater than the state of 50% blockage of this channel and more than the physiological state. Also, the contraction in the state of complete inhibition of the fast potassium channel is more than the state of 50% inhibition of this channel and more than the physiological state according to the results of Table (4). These results indicate an increased contraction in HGWSM tissue compared to the physiological state in potassium channel blockage. In addition, the increase in contraction with potassium channel blockage is greater than the fast potassium channel in HGWSM tissue.

4 Discussions

In this paper, an electromechanical model for human gastric wall smooth muscle is presented based on the electrophysiological interactions of cells with the extracellular environment (via ion channels in the excitable membrane) and the electrophysiological interactions of cells with adjacent cells (via gap junctions). Ions displacement changes the electrical potential difference due to differences in ion concentrations inside and outside the cell environment causes the formation of the action potential. The slow wave is propagated through gap junctions to neighboring cells and eventually to the entire tissue. In this electromechanical model, a cubic geometric arrangement was used to represent the smooth muscle layer of the gastric wall.

Table 3 Percentage of maximal contraction of the electromechanical model of HGWSM tissue in four parts of the gastric body, under two states of potassium channel blockade (half and full) compared to the physiological state.

Part	50% blocked	100% blocked
the beginning of the gastric body	+6.73 %	+17.93 %
the upper part of the greater curvature of the gastric	+6.73 %	+17.51 %
the lower part of the greater curvature of the gastric	+6.74 %	+17.52 %
the end of the gastric body	+7.22 %	+18.24 %

* (Positive sign means more contraction than physiological state)

Table 4 Percentage of maximal contraction of the electromechanical model of HGWSM tissue in four parts of the gastric body, under two states of fast potassium channel blockade (half and full) compared to the physiological state.

Part	50% blocked	100% blocked
the beginning of the gastric body	+6.74 %	+16.11 %
the upper part of the greater curvature of the gastric	+6.74 %	+16.11 %
the lower part of the greater curvature of the gastric	+6.75 %	+16.12 %
the end of the gastric body	+1.27 %	+2.47 %

* (Positive sign means more contraction than physiological state)

The advantages of this model include the following: 1) Finite element approach in electrophysiology. 2) Using a simplified Hill model by considering the contractile and elastic elements as the interface between the nodes. 3) Applying electrophysiological slow-wave to cells and muscles in a physiological state. 4) Investigation of the effect of ion channel blockade on the model. 5) Demonstration and simulation to describe the contractile behavior of tissue in the electromechanical model.

The results in Table (1) for the L-type calcium channel and Table (2) for the T-type calcium channel showed that by blocking of L-type and T-type calcium channels, the amount of tissue contraction in the electromechanical model is reduced compared to the physiological state. According to these results, it was found that complete inhibition of the L-type calcium channel has a greater effect than the T-type calcium channel in preventing tissue contraction (about 1.75%). Also, each channel in 100% blockage has more contraction than 50% blockade in the same channel (about 2% in the L-type calcium channel and about 1% in the T-type calcium channel). In the proposed electrophysiological models for the gastrointestinal tract smooth muscle cell, a decrease in the amplitude of action potential in the spike and plateau phases was observed in the slow-wave curve with blockade of calcium channels [26, 27, 30]. These findings are consistent with the results of the electrophysiological model of gastrointestinal smooth muscle cells. Because blocking calcium channels reduces the slow wave amplitude and reduces contraction [31].

The results showed that the blockage in potassium and fast potassium channels increases the rate of tissue contraction in the electromechanical model compared to the physiological state. Increased blockage in the potassium channel has a greater effect on contraction than in the fast potassium channel. According to the results of Table (3), which is related to the potassium channel, it was found that the effect of 100% blockage of this channel compared to 50% of its blockage is about 11% on the increase of contraction. Also, the results of fast potassium channel blockade show an increase of about 9.5% in tissue contraction compared to 100% and 50% inhibition of the same channel (Table 4). The results showed a greater effect of complete inhibition of the potassium channels on the increase of contraction than complete inhibition of the fast potassium channels by about 1.5%. With the blockage of potassium channels in electrophysiological models of gastrointestinal smooth muscle cells, an increase in the amplitude of the plateau phase in the slow wave was reported [26-28, 30]. These results are consistent with the findings of the electrophysiological model of the cell because the inhibition of potassium channels increases the slow-wave amplitude and indicates an increase in contraction [31]. Pharmacological blockers are used in experimental methods to block the current of calcium and potassium channels in the smooth muscle cells of the gastrointestinal tract. Drugs can be used to block ion channels, control and improve smooth muscle contractions by controlling the influx and outflux of ions through the cell membrane. T-type calcium channel is sensitive to mibefradil and nickel [32, 33], and L-type calcium channel is sensitive to diltiazem, verapamil, and nicardipine [32, 34, 35]. In addition, flecainide and 4-aminopyridine are used to inhibit fast potassium current [36-38], and apamin and tetraethylammonium are used to inhibit potassium current [37-39]. Recently, the effect of these drugs on ion channel blockage in electrophysiological models of gastrointestinal smooth muscle has been simulated [26-28].

Other models proposed by the researchers for the gastrointestinal tract are based on the hollow tubular shape of the organs and the calculation of the stress/strain obtained in solid models [13-17]. In the field of fluids and to study the internal flows of the stomach, scientists designed the gastric wall with artificial indentations and examined the flow paths [18-20]. The difference between this study and other studies is in the details of cell ion channels, the simultaneous effect of electrophysiological and electromechanical interactions of gastric smooth muscles, and the effect of ionic currents on tissue contraction. In addition, the results obtained from the contraction of this model are qualitatively similar to previous research [15, 16].

In addition to the advantages mentioned for the HGWSM electromechanical model, there are limitations to this model. The tissue considered in this model is assumed to be uniform and homogeneous, while the mechanical properties of gastric tissue are heterogeneous and anisotropic [40]. The behavior of the contractile element is assumed to be linear for the HGWSM model. To increase the accuracy of the model, the nonlinear behavior of this component can be simulated using more details such as muscle length change and muscle length change rate. In this model, the effect of electrophysiological stimulation on mechanical contractions of tissue was considered, but the effect of mechanical contractions on electrophysiological interactions was not investigated.
In future studies, these limitations can be reduced by considering various parameters and bringing the model closer to the normal state of the stomach and like heart tissue, different modeling in these fields (electrophysiological, finite elements, circulation, and minimal models) should be presented for Components of the Digestive System and especially the stomach [12, 41-45]. Secondary stimulation can also be performed using electronic chips implanted in the gastric wall to control the gastric wall motility [22, 46].
Finally, using a combination of electrophysiological, electromechanical, and electrochemical modeling for tissues, movement disorders and smooth muscle contraction of the gastrointestinal tract can be improved with the help of pharmacological agents or artificial stimulation of electronic implants.

5 Conclusions

Using electrophysiological and electromechanical models for tissues, the effect of ions is determined on the formation and propagation of slow wave. These models can non-invasively simulate ion channel blockade. The effects of their blockage on different phases of slow wave are determined by the electrophysiological model and the electromechanical model shows slow wave distribution and propagation on the cell layer and tissue contraction. This study quantitatively showed that the blockage of potassium channels and calcium channels leads to an increase and decrease in the contraction of gastric smooth muscle tissue, respectively. By extending this model to more cells, muscle contraction disorders can be simulated more accurately and modulated these defects using pharmacological agents and the bioelectronic implants.

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Nomenclature

C_m	The cell capacitance
D	The voltage propagation function
d	The activation gating variables
E	The Nernst potential
f	The inactivation gating variables
G	The maximum conductance of the channel
$HGWSM$	Human gastric wall smooth muscle
I_{Ca}	The current of the calcium ion channels
$I_{Exchangers}$	The currents of sodium – calcium exchanger
I_{Ca-L}	The general current of the L-type calcium channel
I_{ion}	The sum of all ionic currents
I_K	The current of the potassium ion channels
$I_{Leakages}$	The leakage currents
I_{Na}	The current of the sodium ion channels
I_{Pumps}	The currents of sodium – potassium pump
$I_{Stimulation}$	The stimulus current
$Link$	The interface between the previous and the next node
$Node_i$	Previous node
$Node_{i+1}$	Next node
t	Time
u	The electrophysiological parameters of ion channel gates
V	Cell membrane potential
$\delta_{\text{Contractile}}$	The Change of the contractile component length
δ_{Elastic}	The Change of the elastic component length
δ_{Muscle}	The Change of muscle length
∇^2	Laplacian operator