Chapter 1

Introduction

Mathematics is probably the best discovery of the mankind. It is evident from the fact that mathematical formulations have played a crucial role in unveiling the laws of nature. Physical phenomena are relatively easy to formulate while biological phenomena are a bit difficult to model. Still since experimentations have always some limitations, mathematical intervention for biological investigation may be of immense help. Once such laws are successfully formulated, the mechanism may be used for manmade instruments as engineering application or the understanding may help us get possible remedial measures in case of any dysfunction.

1.1 Peristalsis

Peristalsis is a biological mechanism of pumping fluid in a tube when contraction or expansion waves propagate along the tube wall. Physiological fluids in general are transported by muscular contractions/expansions periodically. Indeed it is an essential biological mechanism accountable for physiological functions of the various organs of the body. Peristaltic pumping is involved in swallowing of food bolus through the oesophagus, embryo transport in the uterus, vaso-motion of blood vessels, spermatic flows in the male reproductive tracts, urine flow through the ureter and also in some other engineering applications. The principle of peristalsis is used to design blood pump in heart lung machines, diabetic pump and roller pumps. The advantage of peristalsis over piston pump is that the contact of the fluid with the machinery components is forbidden. In other words, the purity of a fluid pumped by peristalsis is retained which is not possible with piston pump.

Peristaltic motion observed in physiological flows may be broadly classified into the following three categories (Wright et al., 1982):

- Rush peristalsis,
- Anti-peristalsis and
- Mass peristalsis.

1.1.1 Rush peristalsis

Peristalsis found in different physiological transportations, mainly in the oesophagus and in the small intestine, is termed as rush peristalsis.

1.1.2 Anti-peristalsis

Peristalsis which acts in the opposite direction of the rush peristalsis is referred to as anti-peristalsis. For example, it propagates in the oral direction in the oesophagus. It appears in the second and third parts of the duodenum.

A food bolus is propelled by peristaltic waves of muscle contraction through the oesophagus and into the stomach. Anti-peristaltic waves of contraction are also observed in the oesophagus of some birds and mammals.

1.1.3 Mass peristalsis

Mass peristalsis is a pumping mechanism similar to the rush peristalsis of the small intestines. It is the main action of the large intestine for pumping digested food.

1.2 Physiological systems associated with peristalsis

Peristalsis is a natural cause of transportation of fluids within human and animal bodies. In the human body, it is actively engaged in the motion of fluids in the following systems:

1.2.1 Oesophagus

Human oesophagus is a flexible muscular tube extending from the pharynx to the stomach. Oesophagus is the upper part of the digestive system (Fig. 1.1). The length and the diameter of the oesophagus is as 25-30 cm (Lamb and Griffin, 2005) and 1.8-2.1 cm (Joohee et al., 2012) respectively. Food enters the mouth and when swallowed passes into the pharynx and then enters into the oesophagus. The upper oesophageal sphincter is an inlet meant for regulating the passage of the masticated food bolus, while the lower oesophageal sphincter, also known as cardiac sphincter, acts as an outlet to the abdomen for remaining treatment in the digestive system. The moment a bolus knocks at the upper sphincter, some electro-chemical reactions begin to take place resulting into a message given to the oesophagus and then it gets activated to full distension.

The process of swallowing is a mechanical phenomenon. In the beginning, food is chewed and mixed in the oral cavity and is put into the pharynx which forces the bolus into the oesophagus. The process continues until the bolus enters the stomach by peristalsis through the cardiac sphincter. Contractions and relaxations are not symmetric but absolutely balanced.

The upper oesophageal sphincter is a thickened area of the circular muscle layer of the proximal oesophagus. It prevents reflux of oesophageal contents into the pharynx and passage of air from the pharynx into the oesophagus. The cardiac sphincter is a thickened area of the circular muscle layer of the distal oesophagus, in humans extending over an axial length of 2–4 cm. (Boeckxstaens, 2005).

The peristaltic motion experienced in oesophageal flow is broadly classified into primary peristalsis and secondary peristalsis (Paterson et al., 1991, Mashimo and Goyal, 2006).

1.2.1.1 Primary peristalsis

Primary peristalsis is referred to the swallowing mechanism in which a contraction wave starts from the pharynx and moves down the oesophagus. It involves swallowing reflex, pharyngeal sphincter relaxation, oesophageal contraction and cardiac sphincter relaxation. The propagation of primary peristaltic wave is fastest in the proximal part of oesophagus, and decreases in the middle and the distal part of oesophagus. The average velocity of primary peristalsis in the oesophagus is 4 cm/sec and it takes 10-15 seconds to complete a primary peristaltic activity. The amplitude of contraction wave is largest in the lower oesophagus and smallest in the middle of the oesophagus.

1.2.1.2 Secondary peristalsis

Secondary peristalsis is defined as a physiological mechanism activated by oesophageal distention. It does not involve full swallowing reflex, pharyngeal sphincter and cardiac sphincter relaxations. It is restricted to oesophagus only. Sometimes residual food is seen in the oesophagus due to ineffective primary peristalsis or by refluxed contents from the stomach. This residual food is cleared by secondary peristalsis. It is a local phenomenon which begins just above the point of distension and moves downwards in the oesophagus. Due to distention of the oesophagus, local sensory nerves are activated that causes contraction above the distention and relaxation below it. Secondary peristalsis then proceeds distally, moving the food bolus ahead of it. The propagation velocity and amplitude of these contractions look like those of primary peristalsis.

1.2.2 Intestine

Intestine is a segment of the digestive system extending from the stomach to the anus (Fig. 1.1). The absorption of nutrients and water is done in intestine. In humans, it consists of two segments viz., small and large intestines.

The small intestine in an adult human is about 7 meter long and is approximately 2.5-3 cm in diameter. The small intestine is further subdivided into duodenum, jejunum and ileum while the large intestine is subdivided into caecum and colon.

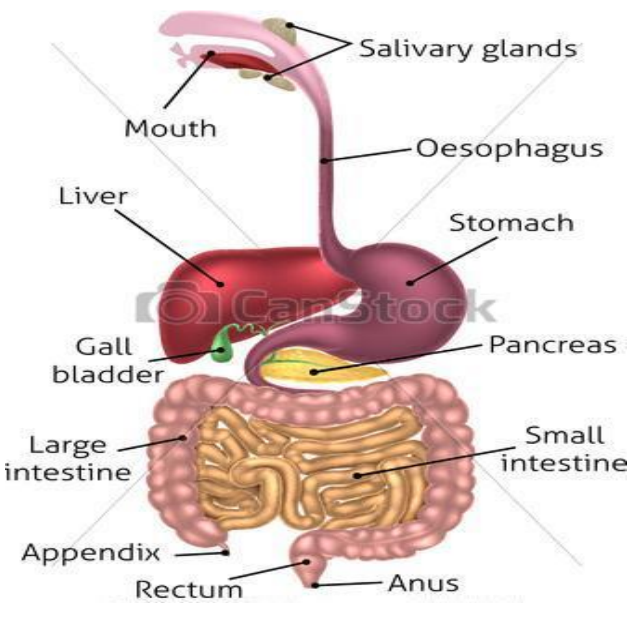

Fig. 1.1 *Human digestive system*
(Courtesy: https://www.canstockphoto.com/anatomical-diagram-digestive-tract-34292934.html)

The large intestine is about 1.5 meter long and about 7.5 cm in diameter. It is the last part of digestive system. The colon part of large intestine absorbs water from wastes of digestive food and creates its into stool.

1.2.3 Ureter

The two long muscular ducts connecting the kidneys to the bladder are known as ureters. In adult humans each ureter is about 30 cm long with the diameter of 4 mm. Ureter collects urine from the kidneys and propels it by peristaltic motion to the bladder against a pressure gradient. At resting tone it is collapsed and gets activated when required to collect waste fluid from the kidneys. When it is fully distended, its cross-section is almost circular while during contraction it takes a star-like shape.

1.2.4 Vas deferens

The long muscular tube originating at the testis near epididymis and connecting to the ejaculatory duct that carry seminal fluid is termed as vas deferens or ductus deferens. Its length in an adult human is about 45 cm. During ejaculation a peristaltic motion occurs in the walls of the vas deferens, thus propelling the seminal fluid forward. The seminal fluid is transported from the vas deferens into the urethra, collecting secretions from the male accessory sex glands such as the seminal vesicles, prostate gland and the bulb urethral glands, which form the bulk of semen.

1.3 Peristaltic pump

Peristaltic pump is a mechanical displacement pump that induces flow in a fluid-filled, flexible polyvinylchloride tube. Peristaltic pump matches the biological process of peristalsis, in which material is moved by the contraction and expansion of smooth muscles in rhythmic waves. It is often used to pump a variety of fluids. The principle of peristaltic pump is based on a mechanism to repeatedly expand a cavity so as to allow fluids to flow into the cavity, and then seal that cavity. The pump works by pressing the flexible tube by rotating wheel attached with adjustable fingers or rollers. There are variety of peristaltic pumps such as blood pump in heart lung machines (Fig. 1.2), diabetic pump, roller pump etc. The advantage of peristaltic pump over piston pump is that the purity of a fluid pumped by peristalsis is retained which is not the case with piston pump.

Fig 1.2 *Blood pump used in heart lung machines*
(Courtesy: https://www.dynetics.eu/ media/1660/japan-servo-blood-pump-2.jpg)

1.4 Bolus formation and swallowing in oesophagus

Formation of bolus and swallowing are an integrated part of the oral actions in the eating process. It involves a series of simultaneous and coordinated contractions and inhibitions of responsible muscles of mouth, pharynx and oesophageal regions. The most important aspect be taken care of during the swallowing process is the ease and safe flow of food boluses through the oesophagus. These physiological processes may be conventionally categorized in three stages as follows (Chen, 2012):

- Oral phase
- Pharyngeal phase
- Oesophageal phase

1.4.1 The oral phase

The formation of a food bolus is a mechanical process and completed with chewing and size reduction, saliva incorporation and other oral actions. For bolus formation, food particles are mixed up with the saliva and moved by the tongue to the back of the oral cavity. The chewing action is not required for a liquid food and oral preparation is relatively simple to solid food. After chewing of solid food and mixing it with saliva and making a portion of the food bolus suitable for swallowing, the oral cavity is sealed between the tongue and the soft palate to prevent the food from leaking into the oropharynx. Now, food bolus is squeezed to oropharynx region by the tongue-palate contact. It is important to care that triggering a swallow should be well-timed. Swallowing of an inappropriate bolus or improper timing may cause coughing, choking and serious health risks during the pharyngeal and oesophagus phases.

1.4.2 The pharyngeal phase

The pharyngeal region is a joint pathway of the gastrointestinal and respiratory tracts through which bolus flow is most complicated. In order to have a safe swallow, the respiratory tracts have to be sealed off and the part of gastrointestinal tract between the oral cavity and oesophagus has to be switched on. The food bolus gains energy and speed during squeezing action of the tongue-palate contact, which forces pharyngeal sphincter to relax and open up to permit the food stuff into the oesophagus. When the tail of the food stuff passes through the pharyngeal sphincter, the pharyngeal phase is accomplished.

1.4.3 The oesophageal phase

After passing through the pharyngeal sphincter, the bolus is moved forward by a series of peristaltic waves propagated along the tube wall in the oesophagus. The propagation speed of this peristaltic wave is fastest in the proximal part of oesophagus, and decreases in the middle and the distal part of oesophagus. It may also be noted that the swallowing of the food bolus in oesophagus is a result of muscle contractions and expansions, and therefore the effect of gravity is almost insignificant to the bolus movement. Once the contraction waves reach down to the cardiac sphincter, it relaxes and permits the food stuff to enter the stomach. Cardiac sphincter is tensioned at resting tone to prevent regurgitation from the stomach and turn out to be relaxed for bolus passing.

1.5 Diseases associated with oesophagus

1.5.1 Hiatus hernia

Diaphragm, which looks dome shaped, separates the abdomen from the chest. The oesophagus passes through hiatus, an opening in the diaphragm, to connect to the stomach. Whenever a part of the abdominal cavity bulges up through the hiatus, the state is referred to as hiatus hernia (Fig. 1.3). A recognized theories of origin is that intra-abdominal pressure increases above the normal to increase the normal gradient between intra-thoracic and intra-abdominal pressure. As a consequece, the oesophago-gastric junction is pushed up into the hiatus (Christensen and Miftakhov, 2000). Due to this bulging oesophagus diverges at the distal end or is a combination of divergence and convergence.

Hiatus hernia often results in heartburn but may also cause chest pain or pain with eating. This condition mostly occurs in people who are over 50 years old or born with an unusually large hiatus. Hiatus hernia may be present with symptoms of oesophageal reflux disease and conversely.

Sliding hiatus hernia and para-oesophageal hernia are the two generally accepted types of hiatus hernia.

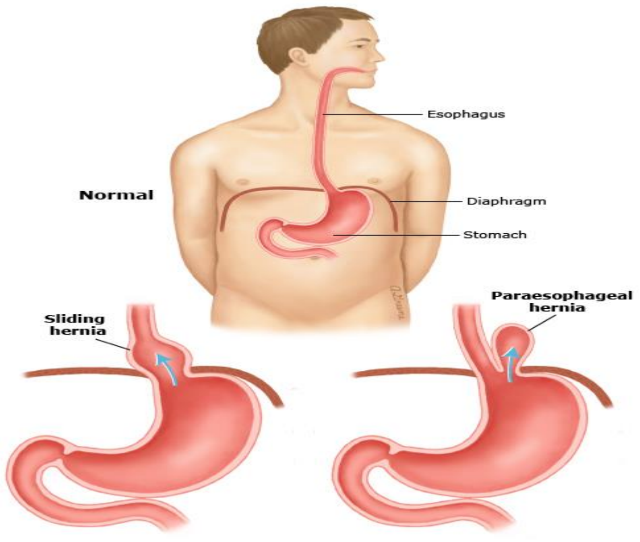

Fig. 1.3 *Normal oesophagus and hiatus hernia*
(Courtesy: https://www.geniemd.net/ penp/Conditions/images /leaflets/hiatal_hernia_pi_edt2_utd.jpg)

1.5.1.1 Sliding hiatus hernia

Sliding hiatus hernia is the common type and is defined as a significant axial prolapsed of a portion of the stomach through the diaphragmatic oesophageal hiatus. It may slide up and down through the hiatus and is usually described as a more than 2 cm separation of the upward displaced oesophago-gastric junction and diaphragmatic impression (Weyenberg, 2013). It usually doesn't cause any serious symptoms and may not require treatment.

1.5.1.2 Para-oesophageal hiatus hernia

In a para-oesophageal hiatus hernia, elements of the abdominal cavity bulge up through the oesophageal hiatus into the part of the thoracic cavity between the lungs and stay there. It is less common (5-15%) of all hiatus hernias. It is serious and may cause blockage of blood flow into stomach.

1.5.1.3 Symptoms of hiatus hernia

Generally no symptoms are experienced by most of patients from their hiatus hernia especially for the sliding hiatus hernia. However, when symptoms are experienced by patients then it usually takes the form of heartburn and regurgitation. This is when the stomach acid refluxes back into the oesophagus. Some patients experience this chronic reflux of acid with fixed hiatus hernias. Hiatus hernia can intensify gastroesophageal reflux by several mechanisms.

The symptoms of hiatal hernia can resemble many disorders. Therefore it is also called the "great mimic". The following symptoms can be experienced by a person with hiatus hernia.

- Pains in the chest
- Shortness of breathing with heart palpitation
- Ingested food "balling up" and causing discomfort in lower oesophagus until it passes on to stomach.
- Several causes of acid reflux
- Feeling sick or being sick
- Mouth filling with saliva

1.5.1.4 Cause of hiatus hernia

It is not always clear why this happens, but pressure on the stomach and age-related changes in diaphragm may contribute to the formation of a hiatus hernia. A person may be born either with an unusually larger hiatus opening or with weak muscle tissue surrounding this opening. Persistent and intense pressure on the surrounding muscles due to vomiting, coughing, straining during a bowel movement or lifting heavy objects may cause hiatus hernia.

Hiatus hernia also caused by:

- Injury to the area
- Pushing up of the stomach by increased intra-abdominal pressure.
- Pulling up of the stomach, due to oesophageal shortening
- Obesity
- Pregnancy

1.5.2 Gastro-oesophageal reflux disease

Reflux of the stomach's contents when back up into the oesophagus cause gastro-oesophageal reflux disease (GERD). GERD is a chronic recurrent condition affecting millions of people. It occurs when the cardiac sphincter is weak or relaxes inappropriately. Sometimes stomach acid, bile acid and pancreatic enzymes regurgitate into the oesophagus and irritate the oesophagus near the heart. Hence, it is called "heartburn". Genetic and environmental factors appear to affect the presence of GERD. Hiatus hernia is a risk factor for GERD symptoms. The individuals with large hiatus hernias have shorter and weaker lower oesophageal sphincters, less-efficient acid clearance, increased amount of reflux and increased severity of oesophagities.

1.5.3 Barrett's oesophagus

Barrett's oesophagus is a precancerous condition in which the normal cells lining the oesophagus transform into an intestinal cell type. These intestinal cells are generally precancerous. Due to gastric contents reflux into the oesophagus over time, the normal squamous cells of the oesophagus are injured. The chronic reflux disease and the presence of bile are critical determinants of the formation of Barrett's oesophagus.

Barrett's oesophagus is diagnosed with biopsies and endoscopy. When the abnormal intestinal cells replace the normal oesophagus, some visible clues indicate the presence of it, but biopsies are definitive. The main treatment option for this condition is to control the reflux disease.

1.5.4 Achalasia

Achalasia is a condition that affects the distal part of oesophagus. The lower oesophageal sphincter is a thickened area of the circular muscle layer of the distal oesophagus. The main function of the lower oesophageal sphincter is to generate a high-pressure and must relax temporarily in order to permit passage of ingested food. Achalasia causes inadequate lower oesophageal sphincter relaxation. As a consequence of inadequate lower oesophageal sphincter relaxation oesophageal clearance is delayed. This leads to a backup of food contents within oesophagus (Spechler and Castell, 2001).

People suffering from achalasia often feel like food is stuck in their oesophagus. Other symptoms may include pain or discomfort in chest and heartburn. Achalasia may occur due to autoimmune condition or may be hereditary. The degeneration of nerves in oesophagus often results to the advanced symptoms of achalasia. A possible treatment for patients with inadequate lower oesophageal sphincter relaxation may be that this is overcome through drugs or operation. Achalasia is treated by dilation or surgical myotomy. Dilatation of achalasia is achieved by complete disruption of the lower oesophageal sphincter.

1.5.5 Nutcracker oesophagus

Nutcracker oesophagus term was given by Castell and colleagues. It is a motility disorder in which hypertensive contraction waves develop in the distal oesophagus during peristalsis (Spechler and Castell, 2001; Ladd et al., 2013). These waves have high amplitudes but maintain their peristaltic pattern. Nutcracker oesophagus results in oesophageal food impaction but it is rare. It is one of the differential diagnoses of the non-achalasia motility disorders of the oesophagus. The main symptoms of this condition are chest pain and dysphagia. High-resolution manometry played a key role in the diagnosis of nutcracker oesophagus.

1.5.6 Oesophageal cancer

Oesophageal cancer develops when the normal working of oesophageal cells go wrong and the cells become abnormal. The abnormal cells keep dividing, making more and more abnormal cells. Oesophageal cancer is becoming more common across the world. Squamous cell carcinoma and adenocarcinoma are the two generally accepted types of oesophageal cancer. Over 95 % of all oesophageal cancers are of these two types. First one develops in the inner layer (mucosa layer) of the oesophagus and second one develops in glandular cells (submucosa layer) of the oesophagus. The cancerous cells may appear anywhere along the length of the oesophagus.

1.5.6.1 Signs and symptoms of oesophageal cancer

There are several conditions that can cause signs and symptoms of oesophageal cancer. The common signs and symptoms of oesophageal cancer are as follows:

- Pain during swallowing
- Heartburn and indigestion
- Back flow of food before reaching the stomach
- Coughing up blood
- Weight loss
- Sticking of food in throat or chest
- Discomfort in the back.

1.5.6.2 Treatment options of oesophageal cancer

Generally treatment options depend on types and stages of oesophageal cancer. Treatment is given to cure the cancer or given with the aim of controlling the cancer and relieving the symptoms. It is treated with surgery, chemotherapy, radiotherapy, cryosurgery or the combination of some of these.

1.6 Types of fluids

1.6.1 Newtonian fluid

A substance which is capable of flowing is termed as fluid. The real fluid for which stress is proportional to the rate of strain, is called Newtonian fluid. The constant of proportionality is known as viscosity. An equation describing Newtonian fluid behaviour is given by

$$\tau = \mu\dot{\gamma},$$

where τ, $\dot{\gamma}$ and μ respectively are shear stress, rate of shear strain and viscosity coefficient.

In other words, a real fluid that obeys the Newtonian law of viscosity is coined as Newtonian fluid. Water, air, mercury, gasoline, light oil and some homemade food items are the examples of the Newtonian fluid.

1.6.2 Non-Newtonian fluid

A non-Newtonian fluid is one that does not obey the Newtonian law of viscosity. The flow curve (shear stress versus shear rate) of non-Newtonian fluid is nonlinear or does not pass through the origin. Its effective viscosity is not constant at a given temperature and pressure but is dependent on flow conditions such as flow geometry, shear rate, etc. Most of the real fluids show as non-Newtonian characteristics. Honey, melted chocolate, custard, toothpaste, some polymer solutions, raisin paste, etc are examples of non-Newtonian fluids.

There are several classes of non-Newtonian fluids. Some of them which are discussed in the thesis are given below.

- Casson fluid
- Power law fluid
- Herschel-Bulkley fluid
- Bingham plastic fluid

1.6.2.1 Casson fluid

The Casson fluid model was originally introduced by Casson (1959) to predict the flow behaviour of pigment-oil suspensions. This model describes the flow of visco-plastic fluids and mathematically described as follows (Bird et al. 1987).

$$\left.\begin{aligned} \sqrt{\tau} &= \sqrt{\mu\dot{\gamma}} + \sqrt{\tau_0}\,, && \tau > \tau_0 \\ \dot{\gamma} &= 0\,, && \tau \le \tau_0 \end{aligned}\right\}$$

where τ_0 is yield stress.

The Casson model is based on a structure model of the interactive behaviour of solid and liquid phases of a two phase suspension.

1.6.2.2 Power law fluid

Power-law model of non-Newtonian fluid is described as (Bird et al. 1987)

$$\tau = \mu|\dot{\gamma}|^{n-1}\dot{\gamma}$$

where μ and n are flow consistency index (effective viscosity $= \mu|\dot{\gamma}|^{n-1}$) and flow behaviour index respectively.

If $n < 1$, the effective viscosity of the fluid diminishes with increasing shear rate and the fluid is called shear thinning fluid (pseudoplastic). If $n > 1$, the effective viscosity of the fluid increases progressively with increasing shear rate and the fluid is called shear thickening fluid (dilatant). The case $n = 1$, is Newtonian case (Fig. 1.4).

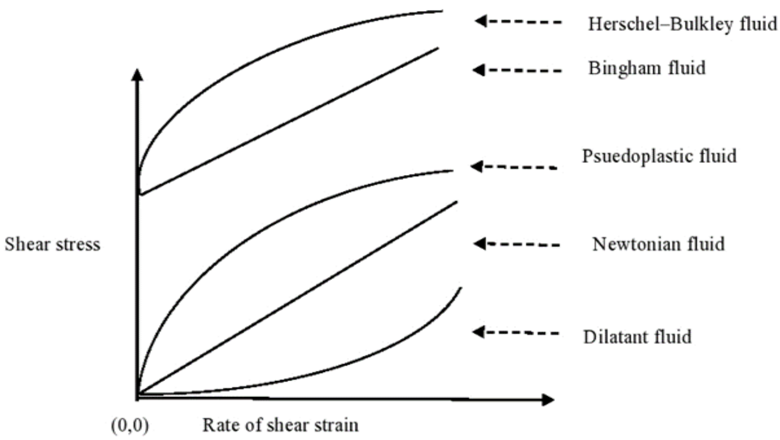

Fig. 1.4 *Pictorial demonstration of Power law fluid and Herschel-Bulkley fluid*

1.6.2.3 Herschel-Bulkley fluid

Herschel-Bulkley fluids are non-Newtonian fluids that possess a yield stress due to which during deformation the fluid has a plug flow region at times when the local shear is below the yield stress. Once the yield stress is exceeded, the fluid flows with a non-linear stress-strain relationship as a shear-thickening or a shear thinning fluid. The Herschel-Bulkley fluid model geometrically presented in Fig.1.4, is defined as (Herschel and Bulkley, 1926)

$$\left.\begin{aligned} \tau &= \mu|\dot{\gamma}|^{n-1}\dot{\gamma} + \tau_0 , & \tau > \tau_0 \\ \dot{\gamma} &= 0 , & \tau \leq \tau_0 \end{aligned}\right\}$$

where τ_0, μ and n are yield stress, flow consistency index (effective viscosity $=$ $\mu|\dot{\gamma}|^{n-1}$) and flow behavior index respectively. Raisin paste, minced fish paste etc. are some examples of edible fluids of this type. This model reduces to Bingham plastic fluid model when $n = 1$.