Research Article

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Colon targeted drug delivery system: Recent approaches.

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Abstract:

The reduction in the systemic toxicity along with high efficiency of local drug delivery for the diseases of colon (crohn's, ulcerative colitis, bowel disease, colon cancer) can be achieved by targeting the colon for drug delivery. Factors such as pH, bacteria, mucus barrier and transit time which affect the efficacy and delivery of the drug, must be considered while developing the targeted drug delivery system. The conventional ways of drug delivery to the colon has its own challenges and obstacles. Thus, the active research area for colon targeting is nanotechnology-based delivery of drugs. Nanotechnology has shown promising results like reduced toxicity, localized drug delivery, improved efficacy and high accumulation in the infected area. But these are also associated with limitations such as uptake of the drug in the upper part of the intestine, entrapment by mucus, variations due to pH, drug degradation by acid/enzyme and burst phenomenon. These compromises the therapeutic efficacy of the novel system. To prevent these obstacles, advancements in the technology of the drug delivery is needed which can provide high therapeutic efficiency. This review tries to explain the conventional methods of colon drug delivery along with the challenges associated with it. The role of novel drug delivery systems and its advances in colon targeting has been discussed along with the future prospects.

Keywords: Colon, Novel delivery, Oral therapeutics, Dual stimuli, Mucoadhesive, Recent advances

Introduction

The prevalence of the colonic disease has increased worldwide in the last few decades, urging the effective treatment strategies of colonic disorders for safe and efficacious drug therapies [1]. The oral drug delivery system is perceived as the most convenient delivery system because of its efficacy and non-invasive process [2]. Thus, oral-based drug delivery system to the colon is a focal point significant to treat varied confined sicknesses such as Ulcerative Colitis (UC), crohn's disease, inflammatory bowel syndrome, and Colorectal Cancer (CRC) [3]. Among colonic infections, Colorectal Malignant Growth (CMG) has caused the most malignant related fatalities in Europe, and is the world's third most diagnosed cancer [1,4]. Even in low-incidence regions such as Asia, the prevalence of Inflammatory Bowel Disease (IBD) is also rising at an alarming rate [5]. Therefore, effective diagnosis and treatment have thus become a major concern in the healthcare sector. The colon-based drug delivery frameworks are built to release the medication specifically into the upper GI tract to the Pulm--monary area without the premature release rate.For the effective advancement of a colon-based delivery system, it is crucial to understand the physiological characteristic of the colon microenvironment encompassing disease site. As the GI tract experiences dynamic changes in the motility, pH and enzymatic action, from the stomach to the digestive system [6]. Colon targeted delivery systems are being actively followed for the local treatment of the colon diseases, since non-targeted conventional therapy may have adverse effects and fewer efficacies due to the absorption of the drug through the systemic route before reaching the targeted site of action [7, 8]. Some of the advantages of the colon based delivery system are shown in Figure 1.

This review portrays a portion of the physiological and obstacles looked by orally managed conveyance frameworks in colon-specific disorders, and the ongoing advancements in orally regulated colon-focused on novel drug delivery system along with the commercial preparations and future research directions in this domain.

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fermentation broth medium which contains 1% (w/v) carbohydrate, bromothymol blue 0.1% as pH indicator in inverted Durham's tube.

Presumptive fungal isolates were further subjected to microscopy using acetone and lactophenol on cotton blue stain placed on a clean grease slide. The cultural and morphological characteristics of the isolates such as hyphae (septation), reproductive structure (sporangia/conidia) in chain or single; the type of spore, etc were observed and served as criteria used for identification [7]. All isolates were confirmed using Microgen™ Identification test kits according to manufacturer's instruction.

Proximate and comparative analysis

The quantitative proximate analysis, as well as comparative analysis of the two food drinks was carried out in the Department of Chemistry, Ahmadu Bello University, Zaria, Nigeria by NCJA and AO. Moisture content was determined drying samples to constant weight as described by [8]. Ash content was determined then by dry-washing in a Muffle Furnace at 500°C [8]. Crude protein, crude fat, crude fibre and carbohydrate were analyzed following the AOAC methods [9].

Sensory evaluation

A 5-point hedonic scale ranging from 1 ("Dislike very Much") to 5 ("Like very Much") was used to evaluate samples organoleptically using parameters such as aroma, colour, taste, acceptability, thickness and flavour. The panel lists were 25 in number and consisted of students and staff members of Bingham University, Karu, Nigeria.

Statistical analysis

Data obtained were analysed using IBM SPSS Version 20. Mean occurences were used to determine the microbial load of various samples. Chi Square was used to investigate the significant difference in the microbial load in the different locations sampled as well as the proximate, comparative and sensory evaluation. Each test was conducted at 95% confidence interval ($p<0.05$).

Result

Except for the Total Coliform Count (TCC), Instant Fura da nono drinks obtained from Maitama district of Abuja significantly had the highest mean microbial count (Table 1). The least TCC, FC, LABC and TAPC were found in samples obtained from Utako, Jabi, Utako and Wuse respectively ($X2=34.41$; $p<0.05$). For the Fura da yoghurt drinks, samples obtained from Wuse had the highest mean microbial count, except for samples from Garki, which had the highest report of TCC ($X2=21.643$; $p>0.05$). The least TCC, FC, LABC and TAPC for fuara da yoghurt food drink were found in samples obtained from Jabi, Gwarinpa Karu and Gwarinpa respectively (Table 1). Seven (7) genera of bacteria (*Staphylococcus, Escherichia, Lactobacillus, Streptococcus, Leuconostoc, Pseudomonas* and *Bacillus*) were isolated from the present study (Table 2); while two species of fungi (*Rhizopus stolonifer* and *Aspergillus niger*) were isolated (Table 3). On comparing the major compositions, no statistical difference ($p>0.05$) was observed in most of the constituents such as crude fat, crude fibre, ash and Carbohydrate. Statistical differences ($p< 0.05$), were however observed in the moisture and crude protein content (Figure 2). Fura da yoghurt was found to have a lower protein content (2.12 ± 0.68%) than Fura da Nono (3.91 ± 0.36%). The proximate composition between between Fura da Nono and Fura da Yoghurt is presented on

Table 1: Mean Microbial count of the two food drink sold in Abuja

Key: A–Jabi (Maple yoghurt); B-Karu (Yogurberry frozen yoghurt); Ca–Utako; Cb-Gwarinpa (Farm fresh yoghurt); Da–Maitama; Db–Garki Area 11 (Shagalinku yoghurt); E–Wuse (Habib yoghurt); CC–Coliform Count; FC–Fungi Count; LABC–Lactic Acid Bacteria Count; TAPC–Total Aerobic Plate Count.

Drink	Location	Mean Microbial Count (Log^{10} cfu/mL)			
Fura da Nono		**TCC**	**FC**	**LABC**	**TAPC**
	A	$3.7x10^5$	$2.27x10^5$	$3.5 x10^6$	$7.9 x10^5$
	B	$2.27x10^5$	$3.34x10^5$	$5.8 x10^6$	$8.3 x10^5$
	Ca	$1.93x10^5$	$4.54x10^5$	$1.5 x10^6$	$7.5 x10^5$
	Da	$2.8x10^5$	$5.34x10^5$	$5.5 x10^6$	$8.8 x10^5$
	E	$3.74x10^5$	$3.54x10^5$	$4.1 x10^6$	$7.4 x10^5$
Fura da Yoghurt	**Location (Yoghurt brand)**				
	A	$0.2x10^5$	$1.6x10^5$	$5.1 x10^7$	$4.2 x10^5$
	B	$0.14x10^5$	$1.1x10^5$	$5.0 x10^7$	$3.8 x10^5$
	Cb	$0.8x10^5$	$0.8x10^5$	$5.5 x10^7$	$3.4 x10^5$
	Db	$1.2x10^5$	$1.4x10^5$	$5.9 x10^7$	$4.8 x10^5$
	E	$0.67x10^5$	$2.14x10^5$	$6.7 x10^7$	$5.3 x10^5$

Table 2: Cultural, Morphological and Biochemical Characteristics of Bacteria Isolated from the 2 types of Food drinks

Colony Morphology							**Biochemical tests**										**Sugar Fermentation**										
Colour	Form	Elevation	Surface	Margin	Microscopy	**Gram Staining**	Catalase	Coagulase	Indole	MR	VP	motility	Gelatin	Oxidase	Spore	Growth @ 4% NaCl	Glucose (A/G)	Lactose (A)	Maltose (A)	Arabinose (A)	Galactose (A)	Sucrose (A/G)	Fructose (A)	Xylose (A)	Mannitol (A/G)	Starch (A)	**Presumptive Isolate**
Light yellow	Circular	Flat	Dull and Rough	Undulate	Single cocci in clusters	+	+	+	-	+	+	-	+	-	-	+	**+/+**	+	+	-	+	+/+	+	-	+/+	-	*S. aureus*
Greyish white	Circular	Raised	Smooth	Entire	Short rods,	-	+	-	+	+	-	+	-	-	-	+	**-/+**	+	-	+	+	+/+	-	-	+/+	-	*E. coli*
White	Circular	Flat	Rough	Undulate	Thick short rods, single or in short chains	+	-	-	-	-	-	-	-	-	-	+	**+/-**	-	+	-	+	+/-	+	+	-/-	+	*Lactobacillus* sp.
white	Circular	Convex	Smooth	Entire	Single cocci in pairs or short chains	+	-	-	-	-	-	-	-	-	-	+	**+/-**	+	-	+	+	+/-	+	+	-/-	-	*Streptococcus* sp.
Cream	Spherical	Flat	Dull and dry	Entire	Cocci, in pairs or clusters	+	-	-	-	-	+	-	-	-	-	+	**+/+**	+	+	+	+	+/-	-	-	-/-	-	*Leuconostoc*
Green	Spherical	Plateaux	Mucold	Entire	Rod	-	+	-	-	-	-	+	+	+	-	+	**+/-**	-	-	+	+	-	+	+	+/+	-	*P. aeruginosa*
Cream	Circular	Low convex	Rough	Irregular	Rod	+	+	-	-	-	+	+	-	-	+	+	**+/-**	-	+	-	-	+/-	+	-	-/-	+	*B. cereus*

Key: A – Acid; G – Gas; + - Positive; - - Negative

Table 3: Cultural and Morphological Characteristics of Fungi in the 2 Food Drinks

Culture	**Morphology**	**Fungal Isolate**
Dark-Brown Mycelium	Dark brown conidia with long conidiophores, map-like Conidiospores and globose vesicles completely covered with biseriate phialides, borne on brown metulae	*Aspergillus niger*
Powdery white appearance with white cotton-like fluffy mycelia	Umbrella-like shape; Non-septate hyphae with rhizoid and coenocytic twin sporangiophore	*Rhizopus stolonifer*

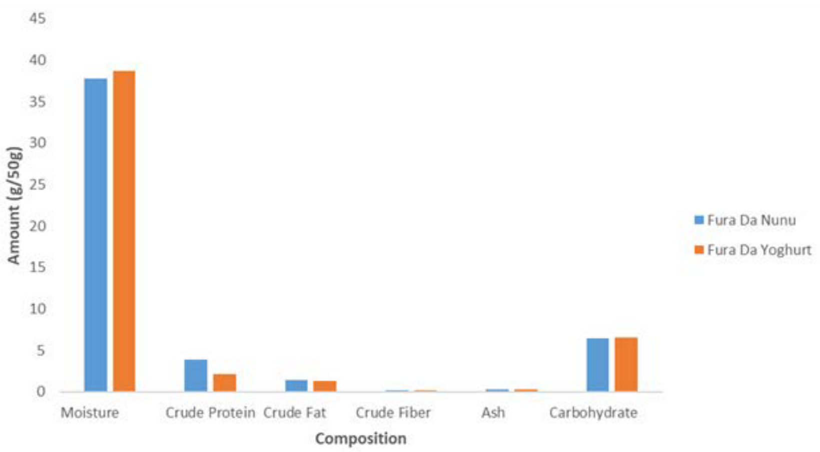

Figure 2: Quantitative comparative analysis of the two food drinks. Experiments were done in triplicates expressed as Mean ± SD.

Composition per constituent (g/50 g):

Fura da Nono: Moisture - 37.83 ± 0.27, Crude Protein - 3.91 ± 0.36, Crude Fat - 1.35 ± 0.25, Crude Fibre - 0.16 ± 0.05, Ash - 0.29 ± 0.03, Carbohydrate - 6.44 ± 0.23.

Fura da Yoghurt: Moisture - 38.76 ± 0.68, Crude Protein - 2.12 ± 0.25, Crude Fat - 1.30 ± 0.16, Crude Fibre - 0.19 ± 0.07, Ash - 0.31 ± 0.01, Carbohydrate - 6.49 ± 0.35.

Figure 3. The composition in percentage for both food drinks are similar, except for the crude protein and moisture content. From the sensory evaluation feedback, the aroma and flavor were significantly higher in Fura de yoghurt (4.6 ± 0.2 and 4.8 ± 0.35 respectively) than in Fura de Nono (3.8 ± 0. 3 and 3.3 ± 0.4 respectively). No significant difference was observed between both food drinks in terms of color, taste, acceptability and thickness (Figure 4).

Discussion

Diet that includes milk products such as the food drinks captured in this study, is a good source of energy, and its consumption helps in elimination of heart problem associated with high cholesterol level in the blood. Calcium and potassium obtained from these food play an important role in regulating and possibly lowering blood. However, yoghurt, as other dairy products, are frequently contaminated by pathogens, which sometimes lead to food intoxication. Health complications associated with consumption of inadequately pasteurized milk products include serious infections that are difficult to treat with antibiotics.

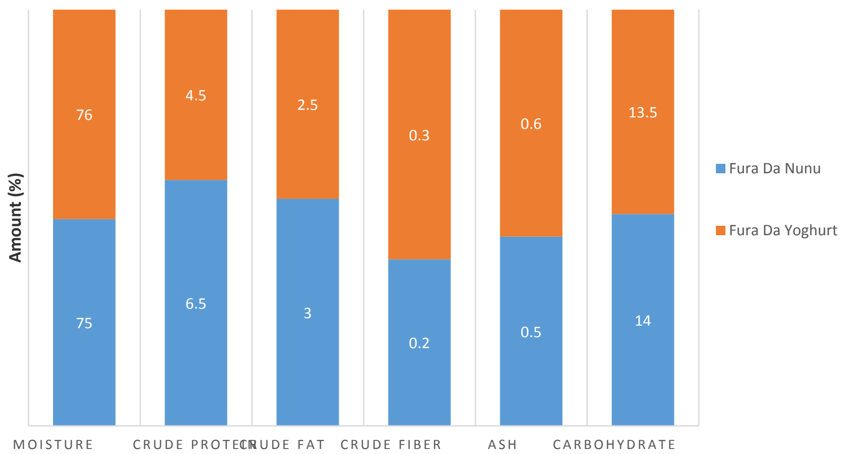

Figure 3: Percentage proximate composition of Fura da Nono and Fura da Yoghurt.

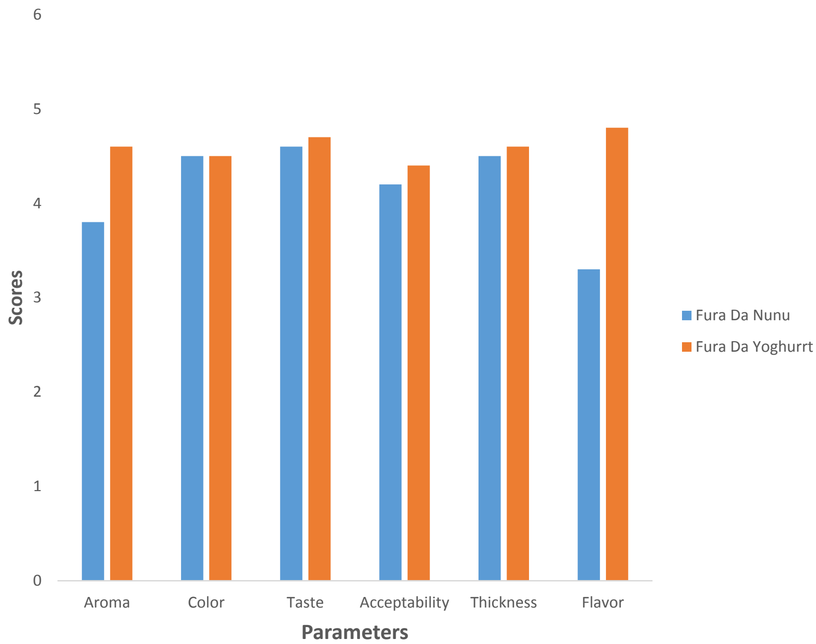

Figure 4: Sample mean of sensory evaluation attributes of the two food drinks.

Experiments were done in triplicates expressed as Mean ± SD. Values Containing different alphabet on the same row are significantly different ($p < 0.05$)

Score per parameter:

Fura da Nono: Aroma - 3.8 ± 0. 3, Colour - 4.5 ± 0.2, Taste - 4.6 ± 0.3, Acceptability - 4.2 ± 0.2, Thickness - 4.5 ± 0.1, Flavor - 3.3± 0.4;

Fura da Yoghurt: Aroma - 4.6 ± 0.2, colour - 4.5 ± 0.3, Taste - 4.7 ± 0.1, Acceptability - 4.4 ± 0.3, Thickness - 4.6± 0.1, Flavor - 4.8 ± 0.35.

Microbiological analysis carried out in the present study revealed the presence of microbes, some of which pose danger to potential consumers. Seven (7) genera of bacteria (*Staphylococcus, Escherichia, Lactobacillus, Streptococcus, Leuconostoc, Pseudomonas and Bacillus*) and two species of fungi (*Rhizopus stolonifer* and *Aspergillus niger*) were isolated. While the presence of *Lactobacillus* and *Streptococcus* in this study was expected as they play key role in the fermentation process of milk to yoghurt; the presence of *Bacillus cereus* is a cause for great concern. *B. cereus* wasn't isolated from any of the instant food drink made from processed yoghurt (Fura da yoghurt), but was observed in Fura da nono–the food drinks made from the locally fermented yoghurt. While *B. subtilis* is a proven fermentation agent [10], *B. cereus* is a pathogen whose spores, when ingested, may lead to food poisoning. It also produces toxins–diarrheal (characterized by diarrhea) and emetic toxin (characterized by nausea and vomiting). The absence of the organism from the food drinks made from industrially processed yoghurt may be due to pasteurization process involved at some point, during the processing. In recent times, microbial contamination is further check mated in high quality yoghurts by either pasteurizing at low temperature, or producing from already pasteurized milk.

Staphylococcus, Escherichia, Leuconostoc, and *Pseudomonas* were reported in all food drinks sampled in the current study. While *Leuconostoc* is an epiphytic organism which plays key role in several industrial and food fermentation as well as impart characteristic flavor; the other microbes are capable of causing food borne infection. Environmental hygiene and handling process may have played a role in the contamination of the food drinks with these organisms. The possibility of transmission/contamination of Fura da nono from the respective animal sources is also not ruled out in this study as the Fulani nomads move about with their cattle, and so, the production process and general observation of HACCP is highly unlikely.

The presence of the two (2) isolated fungi species from this study is in concordance with Oyeleke et al. [11] who reported that moulds to be the major contaminants of yoghurt in Nigeria. Their presence may also have been introduced by the Fura (mashed millet) used to make the food drink mixture. Fungi are known to contaminate plant produce, especially during harvest or post-harvest. *Aspergillus* is known to produce mycotoxin, which exposes consumers to food intoxication [12] while *Rhizopus* is an opportunistic pathogen and one of the most common causative agents of invasive mucormycosis. It also causes zygomycosis, in which fungal infection are seen in face and oropharyngeal cavity. Organisms like *Corynebacterium* and *Listeria* were not isolated in the present study. This could be attributed to the culture media used.

The mean microbial count revealed colony forming units higher than the 1x104 cfu/mL standard that is set for dairy food drinks/beverages under regulations. Higher microbial count was seen for the instant Fura da nono drinks obtained, compared its Fura the yoghurt counterpart. Only the Lactic Acid Bacteria Count (LABC) of all obtained Fura da yoghurt were higher. This is understandable, as *Lactobacillus* and *Streptococcus* are used as starter culture for the industrially processed yoghurt contained in the Fura da yoghurt, and hence, the regulation of inoculum standards by manufacturers, to attain the required standard of 107 cfu/mL [13]. There is no such regulation in the locally processed yoghurt, hence, the lower count observed. The Fura da yoghurt were expected to have little or no contamination, giving the presence of processed yoghurt which is generally believed to be safer. The titre levels observed could however be attributed to post-production contamination, almost open air marketing and other environmental factors, as well as handling procedures by vendors. This invariably means that Fura da yoghurt is not absolutely safe, as generally believed by the patronizing Nigerian customers, unless purchased in hygienic and closed environments like restaurants and malls.

Generally speaking, the highest mean microbial count in Instant Fura da nono obtained from Maitama market. This is surprising, as Maitama district of Abuja is an exclusive area for the top brass and crème de la crème of the society, hence, expected to be less exposed to food contamination and/or food borne infections. It should be noted however, that some of the vendors of instant Fura da nono drink move from one location to another to hawk their products and so, may have carried the samples used for the present study from other more exposed locations. The instant Fura da yoghurt drinks obtained from Wuse market had the highest mean microbial count. This is expected, since the market is the main market in Abuja, and probably the largest, hence, is more exposed to food-borne pathogens which may more easily be introduced into the samples via the unhygienic environment, air, water used to wash the blender and mixing containers; as well as handling processes.

The percentage proximate analysis from the present study revealed Fura da nono to be more nutritious than its Fura da yoghurt counterpart. The industrially processed yoghurt used in the making of the instant Fura and yoghurt drink undergoes pasteurization and other production processes which may lead to the reduction of some of the nutritional components. The result obtained from both drinks is however, in agreement with that obtained by Eruteya and Eze [14]. The carbohydrate and protein content of the two food drinks studied were lower than expected. It could be that the Fura (millet balls) used for the drinks were not freshly prepared at the time of purchase, or some crude carbohydrate might have been lost to production processes. Also, the modern method of raising cow involves some potentially harmful inputs that pass on to the milk, and eventually into the yoghurt; such substances may be the antibiotic medicines and hormones in the feeds which may affect the nutritional content of the end product.

The sensory evaluation showed the Fura da yoghurt samples to be more acceptable and preferable to its Fura da nono counterpart. This could further explain the reason for its higher patronage.

Conclusion and Recommendation

This study revealed that Fura da nono and/or Fura da yoghurt drinks sold in common Abuja markets are unsafe for consumption as they contain microbes which pose the threat of food-borne illnesses, food intoxication and gastroenteritis. However, instant Fura da nono prepared and sold in hygienic and/or non-open air environment serves as a more nutritious food drink than Fura da yoghurt. Since both food drinks are instant, ready-to-eat food that require no further heating or processing, great attention should therefore be given to their microbiological safety to eliminate the health hazard posed to consumers. There is urgent need to implement the HACCP on these almost open-air, local food production centres with the main objective of preventing food contamination and safeguarding public health.

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