ORIGINAL ARTICLE

THE ALIMENTARY AND METABOLISM MARKET IN ROMANIA 1998 - 2018. ANALYSIS AND EVOLUTION

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Abstract

The alimentary tract and metabolism medicines market in Romania has grown significantly over the last twenty years. For this reason, we aimed to analyse the evolution of the drug consumption by volume (units) and days of treatment (DOT). A retrospective study was conducted based on the pharmaceutical data extracted from Pharma & Hospital Report, issued by Cegedim between 1998 and 2018 in Romania. The results of the study have revealed that the highest share (in descending order) in units, concerning the therapeutic groups, belongs to: A02 (drugs for acid-related disorders), A16 (vitamins), A03 (drugs for functional gastrointestinal disorders), A10 (drugs used in diabetes), A05 (bile and liver therapy), A07 (antidiarrheals, intestinal antiinflammatory/antiinfectives). Taking into consideration the product type, generic medicines are dominating in volume. By launching year, established medicines, having enough years of clinical experience, are of greater interest than the others. Furthermore, concerning market layers, the volume is quite balanced between the 3 layers (Bucharest and large cities, medium cities, small cities), but almost 2/3 of the population stays in the 3rd layer that raises questions about the treatment accessibility in small cities and villages. Regarding the antidiabetic market, there is a spectacular growth in the use of antidiabetic drugs (both in volume and DOT). Our study has showed an increasing trend for most of the groups of alimentary tract and metabolism drugs. Measures should be taken by national authorities to encourage prevention, management of drug therapy and rational use of medicines.

Rezumat

Piața medicamentelor destinate tractului alimentar și metabolismului în România s-a dezvoltat susținut în ultimii douăzeci de ani. Din acest motiv, ne-am propus să analizăm evoluția consumului de medicamente la nivel de volum (unități) și zile de tratament (DOT). A fost derulat un studiu retrospectiv cu ajutorul informațiilor farmaceutice obținute din raportul *Pharma & Hospital*, elaborat de către Cegedim între 1998 și 2018 în România. Rezultatele studiului au arătat că, pe grupe terapeutice, cota de piață în volum, în ordine descrescătoare, este reprezentată astfel: A02 (antiacide), A16 (vitamine), A03 (tulburări gastrointestinale funcționale), A10 (antidiabetice), A05 (terapia colecistului si a ficatului), A07 (antidiareice, antiinflamatoare/ antiinfecțioase intestinale). Ca tip de produs, medicamentele generice domină din punct de vedere al unităților eliberate. Conform variabilei „anul de lansare", analiza arată că medicamentele tradiționale, care au suficienți ani de experiență clinică, sunt predominante. Din punct de vedere demografic, volumele sunt bine reprezentate în cele trei direcții (București și orașele mari, orașele medii și orașele mici), dar aproape două treimi din populație aparține celei de-a treia zone; de aceea ne punem întrebarea dacă accesibilitatea la tratament este bună la nivelul orașelor mici și al satelor. În ceea ce privește piața medicamentelor utilizată pentru tratamentul diabetului, am înregistrat o creștere spectaculoasă a utilizării acestor medicamente (volum și zile de tratament). Acest studiu a arătat un trend crescător pentru majoritatea grupelor de medicamente destinate tractului alimentar și metabolismului. Ca și concluzie, autoritățile naționale ar trebui să aducă noi reglementări pentru a încuraja prevenția, managementul terapiei medicamentoase și utilizarea rațională a medicamanetelor.

Keywords: ATC, units, DOT, product type, launching year, market layer, INN, diabetes

Introduction

Diabetes and other alimentary diseases are one of the four major non-communicable diseases (NCDs), which are the leading causes of death worldwide, according to the World Health Organization (WHO) report from 2016 [29]. Consequently, they represent a global burden to the health-care system and one major cause of hospitalization and disabilitation among the elderly and adults. The number of European diabetes patients is estimated to raise from 60 million to 71 million by 2040 [10]. For this reason, several International Nonproprietary Names (INNs) that are found on the List of Essential Medicines 2019 (21st Edition) are used for diabetes treatment [28]. In Romania, the

evolution of antidiabetic drug consumption is of high interest, considering that diabetes mellitus is one of the major mortality and morbidity factors in the country, responsible for 1% deaths in 2016 [30]. Drug usage research is an important part of pharmacoepidemiology, analysing the use of drugs with many consequences in a society [20, 31]. Studies characterizing drug administration patterns are useful to improve therapy, healthcare expenditures, to identify possible drug interactions and to encourage rational drug use [14, 25]. Many reports have generated data on drug sales and use patterns by analysing data based on the World Health Organization Anatomical Therapeutic Chemical (ATC) classification system, Defined Daily Dose (DDD) and WHO core drug prescribing indicators [3]. Moreover, another focus was on the market access of generic medicines representing an instrument in improving patient access to health care, as they provide the same quality, safety and efficacy as the originator drugs, but at lower prices [23]. It is important for authorities to understand the pharmaceutical trends to formulate effective cost strategies and drug treatment policies.

Most studies conducted at the national level evaluated the costs, mostly trends of prescription drugs in general, not focusing on a certain class of medicines. This paper aims to analyse the evolution of the alimentary tract and metabolism drug market in Romania. The study can provide useful information for national policy-makers in order to observe the evolution and prevalence of alimentary tract and metabolism diseases, to increase the rational use of medicines, to elaborate suitable prevention measures and cost-efficacy drug polices, meant to decrease the pressure put on national health-care system by increased drug consumption.

Materials and Methods

We conducted a retrospective study based on information extracted from Pharma & Hospital Report, during a period of twenty years, from 1998 to 2018 a comprehensive pharmaceutical data issued monthly by Cegedim, Romania, starting with 1996. Pharma & Hospital Report represents a statistical estimation of the medicine consumption at the national level, using primary data from a panel of pharmacies.

The analysis has been performed considering: the volume (units), the days of treatment (DOT), by the following variables: ATC code, status, product type, launching year and market layer. The DOT was calculated based on the DDD, updated yearly by the WHO (World Health Organization) Collaborating Center for Drug Statistics Methodology [32].

We have analysed the evolution of the alimentary and metabolism market based on the ATC2 therapeutic groups over the period 1998 - 2018, separated into two decades, and we compared the results obtained for 1998, 2008 and 2018 using as variables: the volume and the DOT. Three market layers were defined and the penetration rate of alimentary and metabolism drugs were established for 2008 and 2018. Additionally, we have presented the antidiabetic market by therapeutic groups and the most prescribed INNs.

Results and Discussion

ATC2 therapeutic groups
According to a report from the National Institute of Public Health, alimentary tract diseases (mostly liver cirrhosis and chronic hepatitis) were responsible for 6% of Romanian deaths in 2019, being observed an increase in mortality (65.2% in 2014 compared with 70.8% in 2019) [16, 17].

Table I

Alimentary tract and metabolism by ATC2 groups – units (millions)

ATC Group	1998	2008	2018
A (ALIMENTARY TRACT AND METABOLISM)	**82.34**	**91.51**	**129.59**
A02 (Drugs for Acid Related Disorders)	9.88	13.98	24.53
A11 (Vitamins)	23.17	18.47	21.01
A03 (Drugs for Functional Gastrointestinal Disorders)	8.70	14.73	15.55
A10 (Drugs Used in Diabetes)	3.76	7.08	14.82
A05 (Bile and Liver Therapy)	7.52	8.58	13.44
A07 (Antidiarrheals, Intestinal Antiinflammatory/Antiinfectives)	4.46	5.81	12.97
A12 (Mineral Supplements)	10.07	10.72	10.55
A06 (Drugs for Constipation)	4.59	3.95	5.84
A09 (Digestives, incl. Enzymes)	3.81	3.33	4.08
A13 (Tonics)	3.64	2.86	2.90
A01 (Stomatological Preparations)	0.93	0.94	2.14
A04 (Antiemetics and Antinauseants)	1.13	0.22	0.92
A16 (Other Alimentary Tract and Metabolism Products)	0.00	0.13	0.77
A08 (Antiobesity Preparations, excl. Diet Products)	0.03	0.38	0.07
A14 (Anabolic Agents for Systemic Use)	0.65	0.33	0.00

In Table I, the evolution in absolute terms is presented to show the increase in several therapeutic groups, considering the number of units (packs) registered in 1998, 2008 and 2018, according to the data extracted

from Pharma & Hospital Report issued by Cegedim, Romania. The alimentary tract and metabolism market, based on the ATC level 2 therapeutic groups, showed the following trends in units (Table I): a significant growth for the groups A10 (Drugs used in Diabetes), A02 (Drugs for Acid Related Disorders) and A07 (Anti-diarrheals, Intestinal Antiinflammatory/Antiinfective); and a moderate growth for the groups A05 (Bile and Liver Therapy).

The results were in line with other studies conducted on elderly patients, showing that the alimentary tract and metabolism drug category was part of the 10 most prescribed drugs [5]. Concerning the drug utilization pattern, the most frequently prescribed drugs are from the sub-class A02, A03 [9, 19, 22]. These findings are similar with the results from Table I, where the highest value based on units was assigned to group A02, the third position being occupied by A03 group. A study

conducted on 600 hospitalized geriatric patients in Pakistan reported that 80% prescribed drugs were for the alimentary tract and metabolic disorders, the highest values being obtained for the following therapeutic groups: A02 – 64.5%, A03 – 21.5%; A01 – 20% and A10 – 19.5% [21]. It can be observed that the drugs from the groups A02, A03 and A10 have been also widely used in therapy by Romanian patients, being in the first 5 groups based on units in 2018, according to the information from Table I. Using DDDs (defined daily dose) as units of measurement, Norwegian Drug Wholesales Statistics highlighted that alimentary tract and metabolism drugs were situated on the second place (512 million DDD), after the cardiovascular drugs [18].

Similar trends with those obtained for units (Table I) are registered in days of treatment (Table II).

Table II

Alimentary tract and metabolism by ATC2 groups – DOT (millions)

ATC Group	1998	2008	2018
A (ALIMENTARY TRACT AND METABOLISM)	**845.40**	**1,043.65**	**1,752.70**
A11 (Vitamins)	432.85	409.91	590.14
A10 (Drugs Used in Diabetes)	68.75	223.27	499.51
A02 (Drugs for Acid Related Disorders)	59.82	192.76	397.05
A03 (Drugs for Functional Gastrointestinal Disorders)	89.49	84.23	99.56
A06 (Drugs for Constipation)	81.69	40.92	46.95
A07 (Antidiarrheals, Intestinal Antiinflammatory/Antiinfectives)	11.20	16.23	32.39
A05 (Bile and Liver Therapy)	7.57	11.06	26.01
A16 (Other Alimentary Tract and Metabolism Products)	0.01	8.37	21.30
A12 (Mineral Supplements)	45.11	17.04	18.92
A09 (Digestives, incl. Enzymes)	10.72	9.94	9.95
A01 (Stomatological Preparations)	14.43	8.75	4.72
A13 (Tonics)	3.81	3.08	3.06
A04 (Antiemetics and Antinauseants)	1.24	0.40	1.96
A08 (Antiobesity Preparations, excl. Diet Products)	0.35	11.00	1.18
A14 (Anabolic Agents for Systemic Use)	18.36	6.69	0.00

An increase over the studied years based on DOT was observed for groups A02, A10 and A07 and a moderate increase for group A05.

In terms of daily doses, studies conducted on geriatric patients also showed that one of the most commonly prescribed drugs was from the alimentary tract and metabolism (25.72%) [9]. Similar results were observed, 29.4% of hospital patients being prescribed drugs acting on the gastrointestinal system: proton pump inhibitors (representing the group A02) counting for 29.4%, followed by antiemetic (19.9%) and laxatives (14.3%) [14]. According to the Norwegian Prescription Database, the most used drugs from group A were pantoprazole 40 mg (5.8%), esomeprazole 30 mg (3.6%) and colecalciferol (2.9%), 10% of the population being prescribed a proton pump inhibitor in 2019. Moreover, it has been observed a moderate growth for group A02 and a constant trend for A05 (bile and liver therapy), A07 (antidiarrheals, intestinal anti-

inflammatory/antiinfective agents) and A09 (digestives, incl. enzymes) [18].

Our results were comparable to the data reported in a study conducted at two facilities in Nigeria. Alimentary tract disorders were reported to be the second most prevalent health problem (16.4%) among 495 patients. Vitamins were the second most prescribed medicines (18.2%) and the first from the alimentary tract and metabolism drugs, the same position for vitamins being observed in Table II, followed by anti-ulcer drugs [3]. Our study identified an increase for acid related disorders drugs between 1998 and 2018 in volume and days of treatment, similar with the trends in proton pump inhibitor use indicated in a study conducted in the United States. It has been reported an increase from 5.70% in 2002 - 2003 to 6.73% in 2016 - 2017, in line with the high prevalence and costs of gastro-oesophageal reflux disease [13].

Status

According to the *Status* criterion, medicines could be split into: Rx (i.e. a medical prescription is required) and OTC (over the counter) drugs.

As shown in Table III, OTC medicines (in units) narrowly lead the market. However, prescription medicines dominated by far the market based on DOT.

Table III

Alimentary tract and metabolism by status

STATUS	UM	Units			DOT		
		1998	2008	2018	1998	2008	2018
Total A	millions	**82.34**	**91.54**	**129.58**	**845.40**	**1,043.68**	**1,752.70**
Rx		28.90	41.31	62.40	365.29	679.75	1245.19
OTC		53.44	50.23	67.18	480.11	363.93	507.51
Total A	%	**100.00%**	**100.00%**	**100.00%**	**100.00%**	**100.00%**	**100.00%**
Rx		35.10%	45.13%	48.16%	43.21%	65.13%	71.04%
OTC		64.90%	54.87%	51.84%	56.79%	34.87%	28.96%

The alimentary tract and metabolism drugs were almost equally split in 2018 between Rx and OTC medicines in units, but Rx accounted for more than 70% in DOT. In the literature, reports on prescription drugs mostly focused on expenditures, in general. For example, in the United States, prescription drug spending increased from $141 billion in 2001 [6] to $325 billion in 2012 [1]. Another information observed from Norwegian Drug Wholesales Statistics was that the Norwegian OTC sale in percentage of total sales in DDD for group A was 22%, after nervous system (489 million DDD) and respiratory system drugs (449 million DDD) [18].

Product type

Drug expenditures have increased globally over the years, and authorities have tried to find strategies to reduce the cost of health care, making drug treatment more affordable to patients [26]. For example, in the United States, total drug spending increased from $279.6 billion (2007) to $307.5 billion (2010) [7, 8]. In many countries, policy-makers introduced measures to promote generic uptake to reduce the burden of drug spending [4, 26]. According to patent ownership, original products are the originators of the patent, while generic medicines (branded or not) are marketed after the originators' patent protection has expired [27]. The data from Table IV shows the following trends: *in units*: increase for generic medicines (in absolute values), although heterogeous between branded (significant increase) and un-branded generics (decrease); a sharp increase for original medicines; *in DOT*: a stagnation for generic medicines, with branded generics to have modest increasing and un-branded generics decreasing (mainly in the first decade); a sharp increase for originals (absolute values).

Table IV

Alimentary tract and metabolism by product type

PRODUCT TYPE	UM	Units			DOT		
		1998	2008	2018	1998	2008	2018
Total A	millions	**82.35**	**91.54**	**129.58**	**845.39**	**1,043.68**	**1,752.70**
Original brands		3.28	9.81	22.63	65.50	282.68	583.78
Branded generics		12.25	22.79	31.88	93.78	300.97	517.92
Un-branded generics		13.38	8.71	7.89	206.00	96.10	143.49
OTC		53.44	50.23	67.18	480.11	363.93	507.51
Total A	%	**100.00%**	**100.00%**	**100.00%**	**100.00%**	**100.00%**	**100.00%**
Original brands		3.98%	10.72%	17.46%	7.75%	27.09%	33.31%
Branded generics		14.87%	24.90%	24.61%	11.09%	28.84%	29.55%
Un-branded generics		16.25%	9.51%	6.09%	24.37%	9.21%	8.19%
OTC		64.90%	54.87%	51.84%	56.79%	34.87%	28.96%

The results concerning the significant increase of original drugs in units and DOT are in line with the finding from other authors. For instance, a study analysing 231 medical records in a tertiary care centre showed that 78.45% prescriptions used original brands [14]. Similarly, Greece had an increased volume market share on off-patent (34.3%) and on-patent (10.6%) originator drugs and a low generic penetration (31.1%), compared to Poland (2.8%, 7.9%, 70.1%) or Portugal (8.3%, 23.6%, 50.3%) [2]. In addition, a Korean study revealed that physicians mostly were prescribing brand-name drugs, even after the implementation of a new pricing policy in 2012, consisting on cutting the price of original medicines, after their patent expired, by 46.45%. Between 2011 and 2013, the originator/generics ratio of use increased to 6.12% [12].

Alternatively, a research conducted in Portugal revealed an ascending trend for volume-based market share of generics, from 31.4% (2010) to 41.4% (2015) and 48.4% in 2018 [15]. A similar trend has been observed for twenty-one European countries in a previous report, indicating a growth for generic drug market share by

volume, between 2006 and 2012 [23]. In the United States, generic prescribing has increased from 19% to 54% between 1984 and 2005, 80% of all prescriptions containing generic medicines. Concerning branded and unbranded generics, twelve countries knew an increase in market share of unbranded generics between 2001 and 2011 (ex. Brazil – 22.3%, Colombia – 19.7%). On the other side, thirteen countries had an increase in market share of branded generics (e.g. Pakistan – 7.1%, Bangladesh – 5.6% and Thailand – 4.9%). Six countries showed an increase in both types of generics (Mexico, Argentina, South Africa, Jordan, Morocco and Philippines). The largest decrease of the

market share (> 6%) for originator medicines were observed in Latin America (Brazil – 20.5%, Mexico – 19.4%, Colombia – 13.2%) [11].

Launching year

Launching year variable displays medicines launched every year.

It is stated that a market is conservative or innovative based on what happened in the first five years after the launching year. A market has the status of innovative market if the consumption in units for the products launched in the last five years represents more than 25% of the total.

Table V

Alimentary tract and metabolism by launching year

LAUNCHING YEAR	Units			DOT		
	1998	2008	2018	1998	2008	2018
Total A	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
Subtotal < 2003	*100.0%*	*65.1%*	*33.6%*	*100.0%*	*68.8%*	*25.5%*
2003		5.1%	3.0%		4.1%	2.6%
Subtotal < 2004	*100.0%*	*70.3%*	*36.7%*	*100.0%*	*72.9%*	*28.1%*
2004		5.1%	1.5%		3.2%	0.7%
2005		11.6%	4.4%		6.9%	2.1%
2006		4.4%	5.0%		4.6%	8.7%
2007		6.0%	3.6%		7.7%	4.1%
2008		2.7%	7.3%		4.6%	12.5%
Subtotal < 2009		*100.0%*	*58.4%*		*100.0%*	*56.2%*
2009			3.8%			2.9%
2010			6.3%			6.7%
2011			9.9%			12.1%
2012			1.4%			1.3%
2013			5.1%			3.6%
Subtotal < 2014			*84.9%*			*82.9%*
2014			6.2%			6.9%
2015			3.5%			4.4%
2016			2.8%			2.6%
2017			2.0%			2.7%
2018			0.5%			0.4%

We could not conduct this analysis before 2003, after this year we noticed three cycles of 5 years each, as follows: *innovative*: the products launched between 2004 and 2008 = 29.8% in units; *innovative*: the products launched between 2009 and 2013 = 26.5% in units; and *conservative*: the products launched between 2014 and 2018 = 15.0% in units. The market changed its innovative profile after 2014, especially due to the regulations regarding Rx price issued in 2015.

Market layer

"Market layer" represents a purchasing behaviour attribute, derived from demographic criteria; three "market layers" were defined: Bucharest and big cities

(university cities or > 250,000 inhabitants); medium cities (50,000 - 250,000 inhabitants); and small cities (< 50,000 inhabitants) and rural areas.

As this attribute was not available in 1998, we analysed only the last decade from this perspective (Table VI). Even if we could not conduct this analysis before 2003, it can be noted that the penetration rate is higher in all three layers.

Although we assume that purchasing habits in important/ medium-size cities include the treatment of certain patients from small cities and rural (parents, grand-parents and other relatives), we can see a certain imbalance between the layers, especially considering the total population of the layers.

Table VI

Alimentary tract and metabolism by Market layer

MARKET LAYER	UM	Units			DOT		
		1998	2008	2018	1998	2008	2018
Total A	millions	**82.34**	**91.53**	**129.58**	**845.40**	**1,043.67**	**1,752.70**
1. Important cities (with universities or > 250.000)		n/a	41.83	49.96	n/a	490.05	685.30
2. Medium-sized cities (50.000 - 250.000)		n/a	25.66	37.11	n/a	292.51	500.71
3. Small cities (< 50.000) & villages		n/a	24.04	42.51	n/a	261.11	566.69
Total A	%	**100.0%**	**100.0%**	**100.0%**	**100.0%**	**100.0%**	**100.0%**
1. Important cities (university or > 250.000)		n/a	45.7%	38.6%	n/a	47.0%	39.1%
2. Medium-sized cities (50.000 - 250.000)		n/a	28.0%	28.6%	n/a	28.0%	28.6%
3. Small cities (< 50.000) & villages		n/a	26.3%	32.8%	n/a	25.0%	32.3%

n/a = not available

Example of details – Antidiabetics

According to data from the National Institute of Public Health, the incidence and prevalence of diabetes have increased. The number of diabetic patients has doubled in the period 2007 - 2014 (from 574196 to 918886 patients) [16], being recorded a total number of 11183671 patients by September 2020 [17].

Table VII indicates the main therapeutic groups in units used against diabetes mellitus, 3 therapeutic groups having more than 80% in the last 20 years: biguanides; sulfonylurea as ADO (oral antidiabetics); insulin as ADI (injectable antidiabetics).

The situation may evolve further, as new therapeutic groups (namely DPP-4 Inhibitor Antidiabetics) were launched in the previous years.

Table VII

Antidiabetics by ATC3 groups

ATC3	Units			DOT		
	1998	2008	2018	1998	2008	2018
Total A10	**3.76**	**7.20**	**15.54**	**68.75**	**231.60**	**520.87**
A10C (Human Insulin and analogues)	1.14	1.33	2.94	14.55	49.26	117.25
A10D (Animal Insulin)	0.41	-	-	1.05	-	-
A10H (Sulphonylurea Antidiabetics)	1.05	2.23	2.84	39.26	73.47	142.60
A10J (Biguanide Antidiabetics)	1.14	3.06	6.75	13.86	90.34	195.31
A10K (Glitazone Antidiabetics)	-	0.21	0.06	-	5.34	1.63
A10L (Alpha-Glucosidase Inhibitor Antidiabetics)	-	0.05	0.13	-	1.54	4.14
A10M (Glinide Antidiabetics)	-	0.11	0.12	-	3.11	3.31
A10N (DPP-IV Inhibitor Antidiabetics)	-	0.00	1.14	-	0.13	22.15
A10P (SGLT2 Inhibitor Antidiabetics)	-	-	0.27	-	-	7.93
A10S (GLP-1 Agonist Antidiabetics)	-	0.00	0.20	-	0.00	5.08
A10X (Other Drugs Used in Diabetes)	0.03	0.21	1.09	0.03	8.42	21.47
Total A10	**100.0%**	**100.0%**	**100.0%**	**100.0%**	**100.0%**	**100.0%**
A10C (Human Insulin and analogues)	30.3%	18.4%	18.9%	21.2%	21.3%	22.5%
A10D (Animal Insulin)	10.9%	-	-	1.5%	-	-
A10H (Sulphonylurea Antidiabetics)	27.8%	31.0%	18.3%	57.1%	31.7%	27.4%
A10J (Biguanide Antidiabetics)	30.3%	42.5%	43.5%	20.2%	39.0%	37.5%
A10K (Glitazone Antidiabetics)	-	2.9%	0.4%	-	2.3%	0.3%
A10L (Alpha-Glucosidase Inhibitor Antidiabetics)	-	0.7%	0.9%	-	0.7%	0.8%
A10M (Glinide Antidiabetics)	-	1.5%	0.8%	-	1.3%	0.6%
A10N (DPP-IV Inhibitor Antidiabetics)	-	0.1%	7.3%	-	0.1%	4.3%
A10P (SGLT2 Inhibitor Antidiabetics)	-	-	1.7%	-	-	1.5%
A10S (GLP-1 Agonist Antidiabetics)	-	0.0%	1.3%	-	0.0%	1.0%
A10X (Other Drugs Used in Diabetes)	0.7%	2.9%	7.0%	0.0%	3.6%	4.1%

The three therapeutic groups with the highest values in units and DOT from Table VII are similar to the ones from a research conducted in Finland between 2003 and 2015. It showed a higher increase for oral antidiabetic drugs in the number of annual purchased DDDs by 87% (from 67 million to 126 million), comparing to insulin – 73% (from 35 million to 61 million). Based on ATC classification, important changes in expenditure share were observed for sulfonylureas (from 2003 – 55% to 2015 – 1%) and thiazolidinediones (from 2003 – 3% to 2015 – 1%), which were replaced with DPP-4 inhibitors (2015 – 62%) [24]. The new therapeutic group (A10N) also registered a significant increase on the Romanian market from 2008 to 2018, in units and especially in DOT (from 0.13 million to 22.15 million), based on the data presented in Table VII.

Table VIII presents the first 10 INNs regarding the oral hypoglycaemic market, ranked according to the descending order (absolute values and % in units) in 2018. Metforminum has been the leading INN for 20 years, but it was a clear trend to treat diabetes with new INN(s) in 2018.

Table VIII

Oral antidiabetics by INN

Rank	INN	Units			%		
		1998	2008	2018	1998	2008	2018
1	Metforminum	0.95	2.32	6.32	43.5%	40.9%	54.9%
2	Gliclazidum	0.15	0.69	1.50	6.8%	12.3%	13.0%
3	Glimepiridum	-	0.95	1.07	-	16.7%	9.3%
4	Sitagliptinum + metforminum	-	-	0.71	-	-	6.2%
5	Metforminum + glibenclamidum	-	0.58	0.43	-	10.2%	3.7%
6	Sitagliptinum	-	0.00	0.33	-	0.1%	2.9%
7	Gliquidonum	0.11	0.10	0.25	5.1%	1.8%	2.2%
8	Dapagliflozinum	-	-	0.22	-	-	1.9%
9	Exenatidum	-	0.00	0.19	-	0.0%	1.7%
10	Glibenclamidum	0.45	0.31	0.01	20.4%	5.5%	0.1%
	Total	**1.66**	**4.95**	**11.04**	**75.9%**	**87.4%**	**95.9%**

Table IX

Injectable Antidiabetics by INN

Rank	INN	Units			%		
		1998	2008	2018	1998	2008	2018
1	insulinum glargine	-	0.17	1.08	-	12.7%	36.8%
2	insulinum aspart	-	0.13	0.57	-	9.7%	19.3%
3	insulinum (human)	1.13	0.88	0.49	73.2%	66.2%	16.6%
4	insulinum detemir	-	0.04	0.35	-	2.9%	12.1%
5	insulinum lispro	0.01	0.08	0.30	0.4%	5.8%	10.2%
6	insulinum glulizina	-	0.04	0.14	-	2.8%	4.8%
7	insulin glargine+lixisenatidum	-	-	0.01	-	0.0%	0.2%
8	insulinum (pork)	0.41	-	-	26.5%	-	0.0%
	Total	**1.55**	**1.33**	**2.94**	**100.0%**	**100.0%**	**100.0%**

In Table IX it is presented the first INNs in the ADI (injectable antidiabetic) market, ranked according to the descending order (absolute values and % in units) in 2018. The most used INN is represented by the *insulinum glargine* in 2018. Both metforminum and *insulinum humanum* were included in the Model List of Essential Medicines (21st list – Ed. 2019) [28].

A report about drug consumption in Norway indicated as the first 10 oral antidiabetics by INN used in 2019: metformin, empabliflozin, sitagliptin, metformin and sitagliptin, dapaglifozin, liraglutide, metformin and vildagliptin, linagliptin, semaglutide, dulaglutide [18]. It can be observed that metformin, sitagliptin, metformin and sitagliptin, dapaglifozin were the most used medicines both in Norway and Romania.

Conclusions

The study provides an overview of the evolution of Romanian alimentary tract and metabolism market. Taking into account the two parameters of analysis, units and DOT, the market has grown significantly over the last twenty years. More patients have been treated for alimentary tract diseases, which represents a positive development.

The results of our study have revealed that, by therapeutic groups, the highest share in units belonged to: A02 (drugs for acid related disorders), A16 (vitamins), A03 (drugs for functional gastrointestinal disorders), A10 (drugs used in diabetes), A05 (bile and liver therapy), A07 (antidiarrheals, intestinal antiinflammatory/ anti-infectives). In addition, one of the leading causes of death and disabilities in Romania, as well as in other European countries, is diabetes, which requires a permanent treatment and care.

Research on the evolution of the national drug consumption provides useful information to authorities to increase the rational use of medicines, in order to maintain sustainable healthcare systems.

Conflict of interest

The authors declare no conflict of interest.

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