

## PŘEHLEDY A ODBORNÁ SDĚLENÍ

### Improving the quality and cost-effectiveness of depression treatment

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#### SUMMARY

##### Improving the quality and cost-effectiveness of depression treatment

Cost of depression treatment in Lithuania increases depending mainly on depression relapse rates. Depression relapse is in a great extent conditional on the quality of health care after the disease was diagnosed. This study was thus aimed to evaluate the first-time depression treatment and antidepressants use according to three specialists groups opinion. For this purpose 361 pharmacists, 317 family doctors and 280 psychiatrists were interviewed in Lithuania in 2009. The data on depression diagnoses were obtained from the Republic Psychiatric Health Centre. The volume of total depression diagnoses grew up by 12% during the period under study (2004–2009), the amount of relapsed depression diagnoses by 27%. According to family doctors' opinion, 13% of respondents still do not initiate depression treatment by themselves and 62% of them refer patients to psychiatrists if depression relapses. Those who prescribe a medicament all alone in most cases use sertraline, but even 38% of family doctors mention benzodiazepines. According to family doctors' answers, 32% of respondents re-evaluate the effect of medicaments in 4 weeks; on the other hand, 25% of them do not carry out such monitoring at all. The obtained results about the differences and efficiency of professional care question the quality of depression treatment in Lithuania. It is therefore necessary to formulate recommendations leading to corrections and rationalization of depression treatment.

**Key words:** depression treatment – antidepressants – depression relapse

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#### SOUHRN

##### Zlepšení kvality léčby depresí a efektivity nákladů s tím spojených

Náklady na léčení depresí v Litvě rostou převážně z důvodu nárůstu recidiv. Výskyt recidivujících depresí je ve značné míře závislý na kvalitě zdravotnické péče následující po diagnostikování depresivního onemocnění. Proto cílem práce bylo hodnocení léčby depresí diagnostikovaných poprvé a používání antidepresiv na základě názorů tří skupin odborníků. Pro tento účel bylo v roce 2009 dotazováno v Litvě 361 farmaceutů, 317 rodinných lékařů a 280 psychiatrů. Data o diagnostikovaných depresích byla získána z Republikového centra psychiatrického zdraví. Za sledované období (2004–2009) vzrostl celkový počet

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diagnostikovaných depresí o 12 %, počet recidiv pak o 27 %. Jak vyplývá z odpovědí rodinných lékařů, jen 13 % z nich si netroufne zahájit léčbu sami; v případě recidiv posílá pacienty k psychiatrovi 62 % lékařů. Ti, co ordinují léčbu samostatně, nejčastěji předepisují sertralin, avšak až 38 % rodinných lékařů uvádí, že používají k terapii benzodiazepiny, 32 % rodinných lékařů vyhodnocuje účinnost medikamentózní léčby po 4 týdnech, na druhou stranu 25 % z nich takové sledování neprovádí vůbec. Získané výsledky o rozdílech a efektivitě odborné péče zpochybňují kvalitu léčby depresí v Litvě. Je proto zapotřebí vypracovat doporučení vedoucí k následné úpravě a racionalizaci léčby tohoto onemocnění.

Klíčová slova: léčba deprese – antidepresiva – recidivující deprese

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### Introduction

Depression ranks among the most common of chronic health problems. It is also associated with higher societal costs than many other chronic diseases, especially in terms of patients' severe limitations in daily functioning and well-being. Despite the existence of medical practice guidelines (which specify the most efficacious therapies for major depressive disorder) patient care varies widely and many patients do not receive appropriate care.

In a series of recent studies, the present authors examined the quality and cost-effectiveness of care for severely depressed patients treated under different payment systems by general medical clinicians and mental health care professionals (psychiatrists, psychologists and master's-level therapists). The conclusion was that overall quality of care for depression is less than optimal, and the cost-effectiveness of care as currently delivered is low. Among seriously depressed patients, many do not receive appropriate care even in the mental health speciality sector, but instead receive care for some problem other than depression or receive treatments that are ineffective for depression. Such mistakes are wasteful of resources: the health care system could get far higher returns for the money it spends treating depressed patients by spending a little more to improve the quality of care – that is, by appropriately treating more of the depressed patients who are already receiving some care anyway. This potential for improving cost-effectiveness of care is especially great for depressed patients who visit general medical providers such as internists or family doctors<sup>1</sup>.

The prevalence of mental disorders in Lithuania reached only 4.6% among total population in 2004, of which 0.6% covered for mood (affective) disorders<sup>2</sup>. These low ratios and the highest suicide rates in Lithuania in the European Region<sup>3</sup> may lead to a discussion whether the recognition and the treatment of depression is sufficient in Lithuania. Consequently it is important to estimate the consumption of antidepressant drugs that are mostly used to treat depressive disorders as well as the costs of depression treatment with medicaments.

Pharmacological aspects of depression treatment have already been assessed for a long time. For example, in 2004, the total expenses of treatment of patients with

various depression forms were estimated to be 118 billion Euros in Europe, or on average 253 Euros per capita per year<sup>4</sup>. Early researches showed that the direct costs for depression treatment accounted for only a small proportion – about 13% – of total amount of disease-related costs. Annual spending on depression in the USA is 43.7 billion dollars, and in England and Wales about 3.4 billion pound sterling. While analysing the costs of disease, all researches showed that the expenses for medicaments accounted for only a small part of the direct costs (10–12%) and only 1–2% of total cost of the disease<sup>5</sup>.

Growing treatment costs encourage to study and assess whether the treatment is reasonable. While assessing the rationality of treatment of this disease, the need of medicaments, psychological support of the patient and cooperation of his/her relatives and the treating doctor is considered.

The costs for the treatment of depression do increase in Lithuania due to the degree of depression recurrence and accounted for 6.95 million Euros of direct expenses in 2009. The growing number of depression recurrence in Lithuania shows the need to analyse the rationality of treatment of primary depression.

The objective of this study is to analyse how three groups of professionals – family doctors, psychiatrists and pharmacists – evaluate the prescription and usage of antidepressants in Lithuania, seeking to rationalize the usage of costs of drug treatment and to suggest measures, how to save funds, while improving the quality of patients' treatment and life, in the future.

### EXPERIMENTAL PART

The data on total sales of antidepressant drugs in all Lithuanian regions over six years (2004–2009) were obtained from IMS (Intercontinental Marketing Service) Health Incorporated. Data were retrieved as units of antidepressant drugs and costs for the drugs. The system and use was quantified in terms of defined daily doses (DDDs). The data were calculated by DDD methodology and expressed in DDDs per 1.000 inhabitants per day. Due to low rates of drug consumption, the Drug

Utilization 95% (DU 95%) was used as the quality indicator of drug prescribing. The number of drugs contributing to 95% of sales as a proportion of the total number was calculated for each year.

In 2009 the following professionals, working in Lithuania, were interviewed: 361 pharmacists or pharmacy technicians (95% CI, n = 5923), 317 family doctors (95% CI, n = 1822) and 280 psychiatrists (95% CI, n = 1030). The confidence level (CL) sets the boundaries of the confidence interval (CI), this is conventionally set at 95% to coincide with the 5% convention of statistical significance in hypothesis testing. A 95% CI is the interval of which you are 95% certain that it contains the true population value as it might be estimated from a much larger study.

Questionnaire survey was selected for data collection: it is perfect for the measurement of quantitative characteristics. The form of the research sample – the so-called available cases: data were collected from doctors and pharmacists, visiting them during their working hours, at their training events, conferences, contacting them in writing and orally, in medical institutions and pharmacies. The primary data were encrypted, using SPSS data processing package Windows/SPSS (Statistical Package for the Social Sciences) 14, and presented with the help of descriptive statistics.

## RESULTS AND DISCUSSION

The findings show that the expenditure of antidepressants (ADs) increased from 22.59 mln Litass (in 2004) to 26.85 mln Litass (in 2008) although it decreased to 23.98 mln Litass in 2009 (Fig. 1). The expenditure decrease in 2009 was based on the antidepressants price decrease because of generic products entering the market. As it is shown, extremely high costs are for SSRIs that include the biggest part of all ADs costs (66% in 2004; 54% in 2009). However, in comparison with the costs of SSRIs, the costs of TCAs are low and declined modestly over the six years (from 1.19 to 0.59 mln Litass). The costs of other ADs raised significantly in a certain period as their consumption had been increased.

In today's cost-conscious environment, suggestions for improving the quality of care are not favourably received because improving quality generally means higher total health care costs. Value of care, or cost-effectiveness, should be an equally important consideration. If, for example, an employee can function much more effectively on the job for a slightly higher investment in treatment, then the benefits accruing to the employer in terms of increased productivity, or to patients in terms of increased income and quality of life, would seem to justify the expenditure. But health plans have little incentive to pick up the tab for increased treatment costs, because plans realize none of these benefits directly, but instead they are under pressure from employers to keep treatment costs down. This research

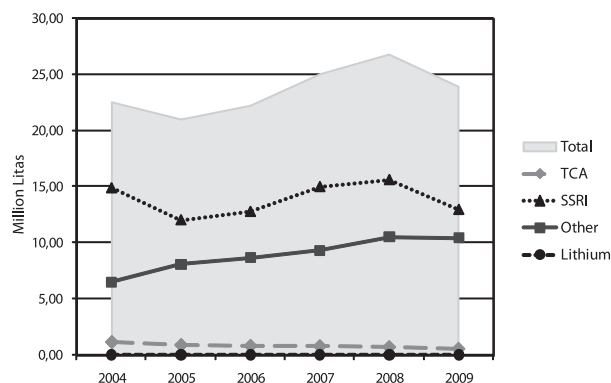


Fig. 1. Costs of antidepressants in six years (2004–2009)

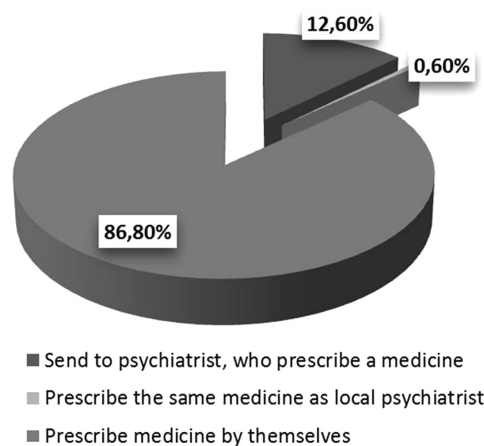


Fig. 2. Family doctors answers to the question: "How do you treat your patients' depression?"

points to the irony of this dilemma and suggests that cost-effectiveness has an important place in the debate.

It should be noted that in 2007 the right to diagnose depression and to prescribe treatment was given to family doctors in Lithuania. According to their responses in the questionnaire, it is evident that in slightly more than one tenth of the cases family doctors refrain from prescription of treatment by themselves (Fig. 2).

While prescribing antidepressants, family doctors usually choose sertraline – a medicament of the SSRI (selective serotonin reuptake inhibitors) class (24.9%), in the second and third place bromazepam (16.7%) and alprazolam (21.2%) – medicaments of the benzodiazepine class – are mentioned (Fig. 3). There were 15 antidepressants molecules in 2009 in Lithuania, the choice of which depends on family doctor's or psychiatrist's decision. However, in accordance with the recommendation of depression treatment and the priority of antidepressants selection in Lithuania, the drug of choice for the treatment of depression should be amitriptyline, unless tricyclic antidepressants (TCAs) are contraindicated in a patient and/or his/her age is under 18 years or more than 65 years. In view of the big proportion of the SSRI drugs mentioned by respondents, the use of antidepressants

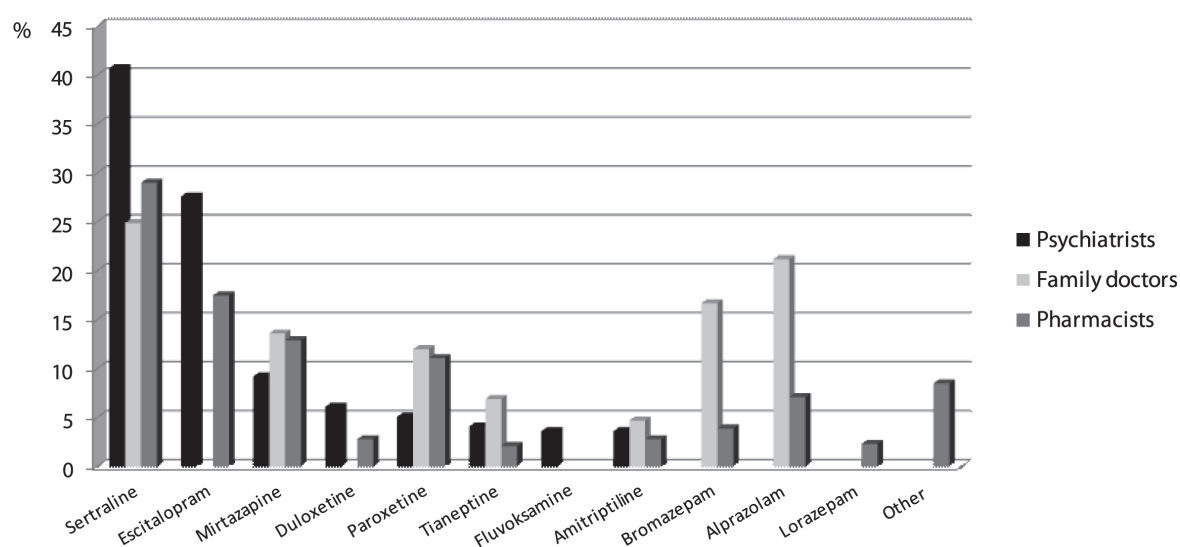


Fig. 3. The most popular antidepressants in family doctors, psychiatrists and pharmacists practice

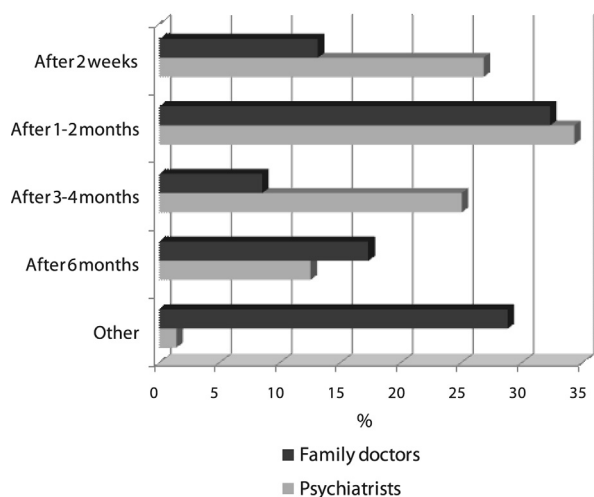


Fig. 4. Monitoring of antidepressants effectiveness by family doctors and psychiatrists

was not consistent with the recommendations for the treatment of depression in Lithuania. Due to high toxicity of TCAs, these antidepressants are used less frequently and for a shorter period than recommended<sup>6</sup>.

After questioning psychiatrists the tendency to prescribe medicine of SSRI group, i.e., sertraline (40.8%) and escitalopram (27.6%), more often showed up, the third most frequently chosen medicine is mirtazapine (9.2%) (Fig. 3).

The survey of pharmacists confirmed the popularity of antidepressants of SSRI class and other more recent antidepressants (Fig. 3). However, it is important to highlight that even 13% mentioned alprazolam, bromazepam and lorazepam, ascribed to the benzodiazepine class. Attention should be paid to the selection of medicaments prescribed for depression treatment by family doctors: the drugs of the benzodiazepine group are not suitable for depression

treatment, they are more often prescribed in the cases of anxiety<sup>7</sup>. The worst is that the preparations of the benzodiazepine class can stimulate suicide<sup>8</sup>.

The next stage of depression treatment after drug prescription is monitoring a patient's condition. When treating the starting or acute depression, the impact of medicine should be noticed after 4 weeks already, and the improvement of the disease course after 8 weeks<sup>9</sup>. A third of the surveyed Lithuanian family doctors indicated that they review the impact of different medicine after 1–2 months, 17% – only after half a year (Fig. 4).

Psychiatrists said that they always or often adjust the dose of medicine for almost half of patients during treatment (27% and 34%, respectively). This emphasizes a higher quality of patient's monitoring by these professionals and higher effectiveness of depression treatment.

The proportion of the cases of depression recurrence is large in Lithuania. Our survey data correlate well with the depression epidemiology data of the State Mental Health Centre. This is confirmed by both surveys of family doctors and psychiatrists: about 35% of respondents of both groups indicated recording the cases of recurrent depression; however, the numbers of cases of recurrent depression differ significantly (Fig. 5).

While analyzing the results of the above responses, conclusions can be made about the working efficiency of family doctors and psychiatrists and the appropriate proposals might be put forward, saving funds and seeking economic and social effect.

After diagnosing a recurrent depression, family doctors refer patients to psychiatrists immediately (61.7% of cases). When meeting the mentioned patients, psychiatrists prescribe the medicament, which has been prescribed earlier, even in 73.36% of cases.

This research suggests that for the improvement of the quality of care for depression it is necessary to raise the value of care and enhance the benefit of treatment dollars. From a patient's perspective, quality improvement leads

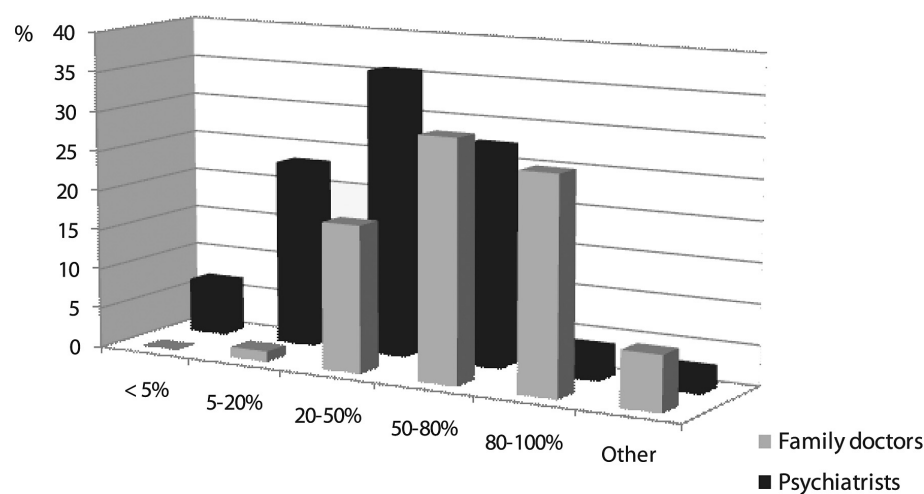


Fig. 5. Relapsed depression frequency in usual practice by family doctors and psychiatrists opinion

to better patient functioning, and this benefit could increase patient's satisfaction, which could be meaningful to plans competing with other plans for enrolment.

The majority of surveyed psychiatrists have a relatively long working experience. However, experienced professionals probably not always evaluate the causes of depression carefully. For example, during this period of physical beauty cult, the cause of depression may be obesity<sup>10</sup>, experienced serious diseases<sup>11</sup>, etc.

When treating a person with recurrent depression, the disease should be looked into even more closely: the reasons for recurrence of depression may be not only inappropriately selected medicament or incorrectly identified diagnosis<sup>12</sup>, but also too early terminated earlier treatment, newly arising psychological problems, the changed social status, etc.<sup>13</sup>. In particular it is important to communicate frequently with the patient, to monitor his/her condition at the beginning of treatment and to react in time, if there are no signs of improvement in appropriate time<sup>14</sup>.

In addition, providing high-quality care that leads to better functioning outcomes creates benefits for many other parties not involved in health care.

The consideration of who benefits from improved quality of care implies, however, that patients and employers would be able to attribute the benefits they accrue from better care to that care, or would otherwise have the necessary information to determine whether a plan or practice that claims to provide higher-quality care actually does so and is worth the additional expense<sup>1</sup>. Unfortunately, this is currently not the case, and better measures of quality and accountability are needed.

## CONCLUSIONS

Recent studies and experience of professionals show that medicaments are not enough for depression

treatment – a combination of an individually selected drug and psychological help is needed. Family doctors and psychiatrists with a long-time experience should re-evaluate the changed context and causes of depression and cooperate more closely with pharmacists, seeking to find out about the latest antidepressants.

The abundance of cases of recurrent depression, especially recorded by family doctors, who have already treated the same patients with depression earlier, encourage to look at the instruction of family doctors to treat this disease anew. It is recommended to provide more information and trainings, regarding depression, to doctors. It should also be encouraged to refer the persons with depression to psychiatrists immediately, in order to avoid a long-term ineffective treatment.

In Lithuania, which is a leader in Europe in terms of suicide rates<sup>15</sup>, it would be useful to look for links of suicide with its frequent cause – depression, and to look deeper into the stories of suicides.

It is the time to evaluate the economic and social impact of depression – treatment costs are exorbitant, but generally not recorded. In the case of the evaluation of this factor, depression treatment would be considered more carefully and responsibly.

## REFERENCES

1. Improving the Quality and Cost-Effectiveness of Treatment for Depression [http://www.rand.org/pubs/research\\_briefs/RB4500-1/index1.html](http://www.rand.org/pubs/research_briefs/RB4500-1/index1.html) (2011.04.18)
2. Data from the State Centre of Mental Health, <http://www.vpsc.lt> (2010.12.10)
3. WHO Highlights on Health in Lithuania, March 2001, [http://europa.eu.int/comm/health/ph\\_projects/1999/monitoring/lithuania\\_en.pdf](http://europa.eu.int/comm/health/ph_projects/1999/monitoring/lithuania_en.pdf)
4. Sobocki, P., Jönsson, B., Angst, J., Rehnberg, C.: Cost of depression in Europe. *J. Mental Health Policy Econ.* 2006; 9(2), 87–98.
5. Neverauskas, J.: Ekonomiškai efektyvus depresijos gydymas [Cost-effective depression treatment]. *Nervų ir*

- psychikos ligos [Nervous and mental diseases], 2003; 1. <http://www.medicine.lt/index.php?pagrid=leidiniai&subid=npl&strid=128> (2011.03.10).
6. **Kavaliauskienė, L., Pečiūra, R., Adomaitienė, V., Masteiková, R.:** Depression relapse and antidepressants consumption in quality of life aspect. *Čes. slov. Farm.* 2010; 59, 199–204.
  7. **Norkus, R., Macevičius, G.:** Benzodiazepinų reikšmė gydant pacientus, sergančius depresija ir nerimo sutrikimais [Role of benzodiazepines in depression and anxiety disorders treatment]. *Nervų ir psichikos ligos* [Nervous and mental diseases], 2007; 6. <http://www.medicine.lt/index.php?pagrid=leidiniai&subid=npl&strid=7016> (2010.08.15).
  8. **Bobrow, R. S.:** Benzodiazepines revisited. *Family Practice* 2003; 20, 347–349.
  9. **Thase, M. E.:** Achieving remission and managing relapse in depression. *J Clin Psychiatry* 2003; 64(Suppl 18), 3–7.
  10. **Luppino, F., de Wit, L., Bouvy, P., Stijnen, T., Cuijpers, P., Penninx, B., Zitman, F.:** Overweight, obesity, and depression: A systematic review and meta-analysis of longitudinal studies. *Arch. Gen. Psychiatry* 2010; 67(3), 220–229.
  11. **Poynter, B., Shuman, M., Diaz-Granados, N., Kapral, M., Grace, S. L., Stewart, D. E.:** Sex differences in the prevalence of post-stroke depression: a systematic review. *Psychosomatics* 2009; 50(6), 563–569.
  12. **Mann, J. J.:** The medical management of depression. *N. Engl. J. Med.* 2005; 353, 1819–1834.
  13. Recovery and relapse prevention. Centre for Addiction and Mental Health. [http://www.camh.net/About\\_Addiction\\_Mental\\_Health/Mental\\_Health\\_Information/Depressive\\_Illness/dep\\_illness\\_relapse.html](http://www.camh.net/About_Addiction_Mental_Health/Mental_Health_Information/Depressive_Illness/dep_illness_relapse.html) (2010.12.17).
  14. What is the general approach to treating depression? <http://www.medicinenet.com/depression/page7.htm> (2010.06.12).
  15. Lietuva pirmąja savizudybių skaičiumi regione [Lithuania is the first in suicide rates in region]. <http://www.vtv.lt/naujienos/nusikaltimai/lietuva-pirmauja-savizudybiu-skaiciumi-regione.html> (2010.06.10)

## NOVÉ KNIHY

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Jej autori Mgr. Fils Andriamainty, PhD., a PharmDr. Ivan Malík, PhD., sú skúsení vysokoškolskí učitelia s viaceročnou praxou v tejto profilovej disciplíne farmaceutického štúdia.

Koncepcia a obsah tohto diela je rozdelený na tri časti.

V prvej sa popisuje príprava, metabolizmus a toxikologické aspekty kyseliny acetylsalicylovej, paracetamolu, metylsalicylátu, fenacetínu, benzokaínu, lidokaínu, trimekaínu, diprofylinu, etofylínu, chlórbutanolu, esterov kyseliny 4-hydroxybenzoovej, sulfanilamidu, ftalylsulfatiazolu, sukcinylsulfatiazolu, fenytoínu, izoniazidu a disulfiram.

V druhej časti sú uvedené ich spektrálne charakteristiky so stručným základom ich princípov a interpretácie so zameraním na IČ, UV/VIS, Ramanových, hmotnostných, NMR spektier.

Tretia časť je venovaná ich základným fyzikálno-chemickým vlastnostiam, ako je rozpustnosť, parametre z chromatografických metód, povrchových javoch, disociačná konštanta, stabilita, rozdeľovací koeficient a reakčná kinetika.

Analýza textu ukazuje, že je napísaný veľmi prehľadne a logicky. Oproti doteraz u nás vydaných analogických učebných pomôcok sa líši najmä tým, že autori do neho zakomponovali najdôležitejšie informácie aj o histórii objavu opisovaného liečiva, priebehu reakčného mechanizmu prípravy, metabolizmu i bezpečnosti práce pri príprave liečiv.

Som presvedčený, že toto dielo vhodne zaplní medzeru, ktorú sme už dlhší čas v tejto oblasti u nás evidovali, pretože je moderne a pedagogicky optimálne koncipovaná učebnou pomôckou.

J. Čižmárik