

Acrylic Custom Made Oral Appliances in Obstructive Sleep Apnea Therapy

ANCA VITALARIU¹, MONICA TATARCIUC^{1*}, DIANA DIACONU^{1*}, LAURA ELISABETA CHECHERITA²

¹ University of Medicine and Pharmacy „Gr. T. Popa” Iasi, Department of Removable Prosthesis Oral Implantology and Dental Technology Prosthesis, 16 Universitatii Str., 700115, Iasi, Romania

² University of Medicine and Pharmacy „Gr. T. Popa” Iasi, Department of Odontology-Periodontology and Fixed Prosthesis, 16 Universitatii Str., 700115, Iasi, Romania

Obstructive sleep apnoea (OSA) is the most common sleep-related breathing disorder that is increasingly recognized as a serious public health issue. The treatment management is determined by the severity of the syndrome. Oral appliances (OAs) are increasingly advocated as a treatment option for mild/moderate obstructive sleep apnoea (OSA). The aim of this paper was to present the two main treatment solutions for OSAS through custom oral appliances made in dental laboratory and to systematically review the available studies in the literature on the efficacy of OAs.

Keywords: Obstructive sleep apnea, Oral Appliances, Heat-curing Acrylic resins, Mandible advancement device, Thermoforming method

Obstructive sleep apnea syndrome (OSAS) is a potentially life threatening condition, characterized by repeated episodes of complete or incomplete obstruction of upper airway narrowing due to their collapse, with micro-weak-ups leading to abnormal sleep, daytime somnolence and seriously cardiovascular and metabolic complications. Population-based studies from the USA, Europe, and Australasia estimate a prevalence of approximately 3–7 per cent in adult middle-aged males and 2–5 per cent in middle-aged females [1]

OSAS common symptoms and signs include: noisy snoring, episodes of apnea during sleep, excessive daytime sleepiness, road or work accidents, headache, dry mouth, high blood pressure, decreased libido, personality changes in or cognitive problems related to chronic fatigue [2].

Accurate diagnosis of OSAS requires Polysomnography, an exploration that require qualified personal and simultaneous tracking of sleep neurophysiologists and cardio-respiratory parameters: nasal/oral air flow, thoracic and abdominal movements, electroencephalograms, electrocardiograms, electromyograms, pulse oximetry, posture and snoring [3].

The treatment management is determined by the severity of the syndrome. OSAS treatment includes drug therapy (respiratory stimulant substances), oxygen administration by Continuous Positive Airflow Pressure (CPAP), surgery and oral devices (OAs) [4]. Although CPAP is a highly efficacious treatment, there is a need for other treatment options because the clinical effectiveness of CPAP is often limited by poor patient acceptance and tolerance, and suboptimal compliance [5]. Oral appliances offer a non-invasive treatment option for patients with OSA, which is considered less cumbersome than CPAP [6]. In certain situations, OAs which are worn intra-orally at night, contribute to upper airway dilation and prevent pharyngeal collapse [7,8]. The American Academy of Sleep Medicine

recommends OA therapy for patients with mild to moderate OSA and for those with more severe OSA who cannot tolerate CPAP and refuse surgery [9].

Oral appliances offer the following benefits: significant reduction in apneas, improvement in sleep, improvement and reduction in the frequency of snoring in most (but not all) patients, few or no complications, they are unobtrusive, make no noise, do not need a power source, and are potentially less costly [10].

A large variety of OAs are available that can broadly be classified as: tongue-retaining devices, soft palate-lifting devices, and mandibular advancement devices (MADs).

Mandible advancement devices (MAD)

MADs are the most commonly prescribed oral devices in the treatment of OSA. They open the airway by bringing the lower jaw forward during sleep and may be recommended in patients with moderate OSAS or patients who cannot tolerate CPAP. There are various types of MADs, the range is given by both the material from which it is constructed and the distance that the lower jaw moves. If the material used is important for the patient's comfort and the device durability, the distance of advance is directly proportional to the increase of the diameter of the cross section of the upper airway. MAD can be *performed*, as „boil and bite”, commercially available, which through a simple procedure adapts to patient with particular dental arch, or *individualized (custom-made)*, requiring the dentist and dental technician. Titratable MADs are designed to gradually protrude the mandible applying an easy-to-use mechanical advancing mechanism, until a protrusive position with positive effect on sleep apnea is reached [11].

Experimental part

The aims of this study were: (1) to present the two main treatment solutions for OSAS through *custom MADs* made

* email: tatarciucm.@yahoo.com; dianadiaconu_vs@yahoo.com

in dental laboratory and (II) to systematically review the evidence on the efficacy of different MADs in the literature. We present both technology and materials used, and their therapeutic efficacy, in terms of the most recent studies in the field, to draw a conclusion about the advantages, disadvantages and efficacy of the two types of therapeutic devices.

Methods of making the custom oral appliances

The methods for making the custom oral appliance are:

a. *Direct method*: tray is built directly on the model by thermoforming procedure.

b. *Indirect method*: involves modeling a wax pattern of the tray that will be converted later in the finished piece of acrylic resins.

Basically, there are two different materials, which are used in the fabrication of the MADs. *Hard acrylic resin* that are either chemically cured or heat/pressure processed, resulting in hard and rigid tooth-borne and occlusal surfaces. Alternatively, there are soft or resilient appliances manufactured from plastics or polymers, producing an appliance which has a somewhat flexible and pliable tooth-borne and occlusal surface [12].

Acrylic resins are known as polymethyl methacrylate or PMMA, which are synthetically obtained and can be packed or injected into molds during an initial plastic phase, which solidify through a chemical reaction of polymerization. The disadvantages of heat-cured acrylic resins connected to increased porosity, high water retention, volume variations and irritating effect of the residual monomer, difficult processing, together with the polymer development, have led to alternative materials such as polyamides (nylon), acetal resins, epoxy resins, polystyrene, polycarbonate resins etc.

The thermoplastic appliances are usually manufactured through *thermoforming procedure* from two kinds of material: (a) Essix type 'A' co-polyester (Raintree Essix, Inc., Metairie, LA, USA) and type Endure (Great Lakes Orthodontics, Tonawanda, NY, USA) and (b) polypropylene co-polymer or ethylene Essix type 'C'+ (Raintree Essix, Inc., Metairie, LA, USA). Resiliente thermoplastic materials are also used, such as Raintree Essix C+, Invisacryl C. There can be found multiple variations in thickness and shape of the materials [12].

There are many types of machines for processing thermoplastic materials with the same working principle, and similar elements: a suction base (in the form of perforated plate or drum of granules) connected to a vacuum source, a supply heat source, a metal frame for mounting thermoplastic film. Complex devices present a mobile arm set for repositioning and the models in occlusion (fig. 1).

Making a MAD using vacuum-thermoforming method

Method of production of the trays consists in lamination by vacuum-thermoforming of a thermoplastic sheet and



Fig.1. The vacuum-thermoforming device (Erkodent/Erkodent Pfalzgrafenweiler, Germany)



Fig.2. Making a DAM using vacuum-thermoforming method

its perfect adaptation to a model. Thermoplastic films used for the MADs are required to be manufactured from vinyl acetate, water-insoluble, biocompatible, and fits perfectly on model after lamination and have a good mechanical strength.

Technological steps are: dental impressions and plaster models realization; positioning the model on the basis of the suction; thermoplastic film adaptation on the; activating the power source and set operating time (60 s); when heating resistance reaches an optimum temperature, it is applied over the frame and it is maintained for 10 seconds until film lamination. Plasticized foil forms a concavity, which increasing and becomes evidently under the frame, this form indicating the optimum moment for applying the foil over the model; vacuum pump is started and maintained for 10 - 20 seconds to achieve a perfect adaptation of the film, by suction the air between film and model; simultaneously, mobile arm descends to reposition the antagonist model in occlusion; the MAD is removed from the model by traction and film excess is cut off, for a good adaptation in cervical area; finally a breathing slot is milled in anterior area (fig. 2);

Making a MAD using acrylic resins through indirect method

The most used material in dental laboratories is represented by heat-cured acrylic resins.

The MAD is made on a model obtained by the impression of patient dental arch (fig. 3). A wax pattern is obtained by lamination of a pink wax sheet 2 mm thick, that requires adjustment on cast. Wires of metal at 0.70 mm diameter are used to make six hooks, two for maxillary and four for mandibular one, that snaps into the wax at canine's maxillary and at molars mandible area.

The process of transforming wax pattern into finite device comply the algorithm for obtaining specific acrylic prosthetic devices through thermal polymerization, following the manufacturer's recommendations. The type and parameters of curing procedure influence the mechanical resistance and the biocompatibility of the final device. Usually, the polymerization of the heat-curing acrylic resins is done at 100°C, in a water bath.



Fig.3. The MAD wax pattern on the model



Fig.4. The two oral appliances are colligating by two rubber orthodontic rings

After the polymerization the two oral appliances are colligating by two rubber orthodontic rings, thus producing a mandible flexible and comfortable advancement in positioning, without restricting freedom of movement of the mandible (fig. 4).

Systematic review of the literature

In order to identify studies relevant to the field of oral appliances treatment for OSA, a computerized database search was carried out using Medline/Pubmed and Embase. The keywords applied in the initial search were "Obstructive Sleep Apnea", "Dental Devices", "Oral Appliances", "Mandibular Advancement Device". Our search was limited to human studies conducted between 2000 - 2014 and language limitations were set to English, French and German. Systematic reviews, meta-analyses and randomized controlled trials (RCTs) with more than 20 adults with OSA were eligible for inclusion. All included studies were exclusively focusing on MAD therapy as OSA treatment modality and were assumed to represent valid information regarding the efficiency of these devices. The reference lists of papers deemed eligible were searched manually for additional relevant publications, which were added to the list of potential studies to be included in this review.

Papers were reviewed and grouped according to the following: (1) studies on the MADs efficacy, (2) studies on the MADs side effects. All papers not specifically falling into one of these outcome groups were excluded from the list of potential eligible studies.

For the efficacy of MADs, objective (Polysomnography) and subjective (Epworth Sleepiness Scale, Functional Outcomes of Sleep Questionnaire) parameters were assessed. Treatment was considered successful when the Apnea-Hypopnea Index (AHI) was < 5 or showed substantial reduction, defined as reduction in the index of at least 50% from the baseline value to a value of < 20 in a patient without OSAS symptoms while undergoing therapy.

Results and discussions

Our research revealed initially 335 articles from the primary database searches, of which only 43 meet the criteria for inclusion. All the rest were excluded as the studies were not limited to MAD as the treatment modality of OSA, their efficacy and side-effects. The reviewed studies provided some detail on the design of the MAD used; however, some were more specific than others. Five studies used commercially available appliances [13-17], and all the rest used custom-made MADs.

Efficacy of MAD in the management of OSA

Thirty studies were included in this group. Few studies found poor results or just some little improvements [18]. Polysomnographic criteria with AHI less than 10 per hour has been noted in certain cases, although no improvement or even worsening was noted in other cases [19-21]. Most of the studies reported a significant reduction between

baseline and follow-up AHI/RDI for patients wearing a custom-made MAD [2, 9, 10, 14, 16, 22-36] According to the predetermined success criteria, complete response was defined as a resolution of symptoms and a reduction in AHI to less than 5 per hour, and partial response was defined as improved symptoms and a reduction in AHI of 50% or more, with the AHI remaining at a value of 5 or more per hour. In a study of Pitsis, the custom-made MAD was shown to significantly improve AHI results, for 74 per cent of patients the treatment being completely successful and partially successful in 61 per cent. Only two studies found a significant difference between the two MADs tested [25]. Vanderveken found that a custom-made monobloc MAD significantly improved subjects' AHI ($P < 0.01$) when compared with a commercially monobloc MAD [16]. The custom-made MAD resulted in significantly higher treatment success (60 versus 31 per cent; $P < 0.05$). The same conclusion was found by Rose, who compared two MADs, one custom-made and one commercially available [13]. Interesting is that although most reviewed studies analyzed the success of the treatment in mild to moderate OSA patients, one study found that MAD reduced AHI significantly in severe OSA subjects with favorable responses, from 49.3 (37.4-67) to 12.5 (6.1-15.7), $p < 0.001$ at 3 months and from 47.5 (41.1-72.9) to 13.1 (6.0-14.0), $p < 0.001$ at 1 year [37]. The majority of studies showed that MAD have effect on polysomnographic indices (AHI or RDI) highlighting that mandible advancement is crucial to the efficacy of these oral appliances. There is a relationship between the degree of advancement of mandible and the efficacy of MADs as those with greater mandible advancement proved to be more efficient in improving polysomnographic indices [20, 38].

Side effects of MADs

Almost every study describing MADs comments on the side effects voiced by patients. Fifteen studies specifically focused on the side effects and compliance with treatment, while others simply asked a few questions about the side effects. Table 1 summarizes some of the common side effects. Excessive salivation, dry mouth, and teeth discomfort are the most common side effects reported, but they were considered minor and transient symptoms [8, 17, 22, 39-41]. The dental-skeletal effects of MADs are certainly present, but the long-term results and their clinical significance are unknown at this time. Two studies of Marklund and Almeida described patients who were using MADs for more than 5 years. Their results suggest that orthodontic changes are variable (favorable in some patients and unfavorable in others), are clinically relevant, and might be predictable from the initial dental characteristics of the patients and the type of device [20,38]. Significant dental changes after a long-term use reported Doff in his controlled study, too [42]. Some changes in mandibular posture were reported by Almeida [38] after a long-term use (more than 5 years) and transient pain in TMJ were found by Birleanu [29] and Doff [43] in their

Side effect	Period	% of patients	Reference
excessive salivation	14-36 month	12.5%	39
	12-30 month	55%	22
dry mouth	14-36 month	12.5%	39
	12-30 month	86%	22
	> 3 years	30%	44
tooth discomfort (tenderness)	14-36 month	12.5%	39
	12-30 month	59%	22
	> 3 years	38%	44
Teeth position and occlusion changes	2 years	17%	26
	> 5 years	44,3%	21
	2 years	28%	33
	> 3 years	40%	44
jaw discomfort	14-36 month	12.5%	39
	12-30 month	41%	22
	> 3 years	50%	44
TMJ discomfort	2 month	24%	43
	> 3 years	30%	44
Mandibular posture changes	> 5 years		38

Table 1
THE MOST COMMON REPORTED
SIDE EFFECTS OF ORAL
APPLIANCES

studies. At the 2-year follow-up Fransson found significant changes in the mean mandibular range of protrusion (+0.6 mm), overjet (-0.5 mm), and overbite (-0.8 mm) were registered. Nine of the 65 patients had developed a lateral open bite, and 2 were aware of the change [26]. In a long-term clinical study (more than 3 years) of the acrylic MADs, Clark found that patients reported 50% jaw/facial muscle pain, 40% occlusal changes, 38% tooth pain, 30% reported TMJ pain and 30% experienced xerostomia [44-46]. Annual follow-up office visits with the dentist appear necessary for early detection of these changes.

A comparison of the studies is difficult as the definition of treatment success varied greatly. Studies in this review defined success as a reduction of AHI/RDI either by 50 per cent, below five events per hour, or below 10 events per hour, and some defined success as patient satisfaction. Therefore, depending on the definition of success/failure criteria, the rates of reported success may be biased and different from study to study. Deductions regarding whether materials used in the fabrication of the oral appliances influence treatment outcome cannot be made as there are no studies specifically investigating this issue [47-53].

Conclusions

Oral appliance design has been suggested as one of the factors that will affect treatment success, adherence, and side effects.

Prefabricated, made out of thermoplastic material can be fitted chair-sided, preferably by a dental sleep professional at the outpatient clinic. Researches showed that this type of MADs have limited effectiveness.

Custom-made MADs fabricated in a dental laboratory from individual impressions of a patient's tooth arches are better tolerated and provide a higher efficacy compared to prefabricated appliances.

All MADs proved successful in improving AHI/RDI and suggest that mandibular advancement is crucial in terms of establishing efficacy.

The systematic reviews consistently concluded that MAD are less effective than CPAP when AHI is used as the outcome of interest, but are better tolerated by the patients. Adverse events among patients with MADs were common, but mostly mild and transient.

It is as yet unclear which type of MAD will bring about the desired treatment effect for patients with OSA, and further research comparing different appliances and different designs and materials is needed to shed light on this issue.

References

- AHRENS, A., McGRATH, C., HÄGG U., *European Journal of Orthodontics*, **33**, 2011, p.318.
- HOEKEMA, A., STEGENGA, B., WIJKSTRA, P.J., VAN DER HOEVEN, J.H., MEINESZ, A.F., DE BONT, L.G., *J Dent Res.*, **87**, No. 9, 2008, p.882.
- PADMA, A., RAMAKRISHNAN, N., NARAYANAN, V., *Indian J. Dent. Res.*, **18**, No. 4, 2007, p.201.
- BASNER, R.C., *N. Eng. J. Med.*, **356**, No.17, 2007, p.1751.
- CHAN, A.S., CISTULLI, P.A., *Curr. Opin. Pulm. Med.*, **15**, No.6, 2009, p.591
- HOFFSTEIN, V., *Sleep Breath.*, **11**, 2007, p.1.
- KUSHIDA, C.A., MORGENTHALER, T.I., LITTNER, M.R., et al., *Sleep.*, **29**, 2006, p.240 .
- FERGUSON, K.A., CARTWRIGHT, R., ROGERS, R., SCHMIDT-NOWARA, W., *Sleep.*, **29**, 2006, p.244.
- LIM, J., LASSERSON, T.J., FLEETHAM, J., WRIGHT, J., *Cochrane Database Syst Rev.*, **25**, 1, 2006, CD004435.
- NG, A., GOTSPOULOS, H., DARENDELILER, A.M., CISTULLI, P.A., *Treat Respir. Med.*, **4**, No. 6, 2005, p.409.
- DIELTJENS, M., VANDERVEKEN, O.M., HEYNING, P.H., BRAEM, M.J., *Sleep Med Rev.*, **16**, No.2, 2012, p.177.
- CHECHERITA, L., BELDIMAN, M.A., STAMATIN, O., FOIA, L., FORNA, N.C., *Revista de Chimie (Bucharest)*, **8**, 2013, p.864.
- ROSE, E.C., STAATS, R., VIRCHOW, C., JONAS, I.E., *Eur. J. Orthod.*, **24**, No. 2, 2002, p.191.
- VANDERVEKEN, O.M., BOUDEWYNS, A.N., BRAEM, M.J., *Acta Otolaryngol.*, **124**, No.5, 2004, p.628.
- GAUTHIER, L., LABERGE, L., BEAUDRY, M., LAFORTE, M., ROMPRÉ, P.H., LAVIGNE, G.J., *Sleep Medicine.*, **10**, 2009, p.329
- VANDERVEKEN, O.M., DEVOLDER, A., MARKLUND, M., et. al., *Am J. Respir. Crit. Care Med.*, **178**, No. 2, 2008, p.197.
- TSUDA, H., ALMEIDA, F.R., MASUMI, S., LOWE, A.A., *Sleep Breath.*, **14**, No. 3, 2010, p.227
- SMITH, D.M., STRADLING, J.R., *Thorax.*, **57**, No. 4, 2002, p.305.
- PETITJEAN, T., LANGEVIN, B., IDRISSE, S.M., PHILIT, F., GARCIA TEJERO, M.T., ROBERT, D., *Rev. Stomatol. Chir. Maxillofac.*, **103**, No.3, 2002, p.170.
- MARKLUND, M., *Am. J. Orthod. Dentofacial Orthop.*, **129**, No.2, 2006, p.214.
- ALMEIDA, F.R., LOWE, A.A., SUNG, J.O., TSUKI, S., OTSUKA, R., *Am. J. Orthod. Dentofacial Orthop.*, **129**, No.2, 2006, p.205.
- FRITSCH, K.M., ISELI, A., RUSSI, E.W., BLOCH, K.E., *Am. J. Respir. Crit. Care Med.*, **164**, 2001, p.813.
- ROSE, E.C., BARTHLEN, G.M., STAATS, R., JONAS, I.E., *Am. J. Orthod. Dentofacial Orthop.*, **121**, No.3, 2002, p.273.
- ROSE, E.C., GERMANN, M., SORICHTER, S., JONAS, I.E., *J. Orofac. Orthop.*, **65**, No. 6, 2004, p.489.

25. PITSIS, A.J., DARENDELILER, M.A., GOTSPOULOS, H., PETOCZ, P., CISTULLI, P.A., *Am. J. Respir. Crit. Care Med.*, **166**, No. 6, 2002, p.860.
26. FRANSSON, A., *Swed Dent. J. Suppl.*, **163**, 2003, p.1.
27. AARAB, G., LOBBEZOO, F., WICKS, D.J., HAMBURGER, H.L., NAEIJE, M.J., *Oral Rehabil.*, **32**, No.8, 2005, p.64
28. MACHADO, M.A., JULIANO, L., TAGA, M, de CARVALHO, L.B. do PRADO, L.B., do PRADO, G.F., *Sleep Breath.*, **11**, No.4, 2007, p.225
29. BÎRLEANU, L.A., RUSU, G., MIHAESCU, T., *Pneumologia.*, **58**, No. 4, 2009, p. 226.
30. CHAN, A.S., CISTULLI, P.A., *Curr Opin. Pulm. Med.*, **15**, No.6, 2009, p.591 .
31. LAM, B., SAM, K., MOK, W.Y., et al., *Thorax.*, **62**, 2007, p.354.
32. SUTHERLAND, K., CISTULLI, P., *Swiss Med Wkly.*, **28**, 2011, p.141.
33. DOFF, M.H., HOEKEMA, A., WIJKSTRA, P.J., VAN DER HOEVEN, J.H., HUDDLESTON SLATER, J.J., DE BONT, L.G., STEGENGA, B., *Sleep.*, **36**, No. 9, 2013, p.1289.
34. DIELTJENS, M., BRAEM, M.J., VROEGOP, A.V., WOUTERS, K., VERBRAECKEN, J.A., De BACKER, W.A., Van de HEYNING, P.H., VANDERVEKEN, O.M., *Chest.*, **144**, No.5, 2013, p.1495 .
35. ALMEIDA, F.R., MULGREW, A., AYAS, N., TSUDA, H., LOWE, A.A., FOX, N., HARRISON, S., FLEETHAM, J.A., *J. Clin. Sleep Med.*, **9**, No. 4, 2013, p.319.
36. KRISHNAN, V., COLLOP, N.A., SCHERR, S.C., *CHEST.*, **133**, 2008, p.1135
37. LAM, B., SAM, K., LAM, J.C., LAI, A.Y., LAM, CL., IP, M.S., *Sleep Breath.*, **15**, No.2, 2011, p.195 .
38. ALMEIDA, F.R., LOWE, A.A., SUNG, J.O., TSUIKI, S., OTSUKA, R., *Am. J. Orthod. Dentofacial Orthop.*, **129**, No. 2, 2006, p.195.
39. HAMMOND, R.J., GOTSPOULOS, H., SHEN, G., PETOCZ, P., CISTULLI, P.A., DARENDELILER, M.A., *Am. J. Orthod. Dentofacial Orthop.*, **132**, 6, 2007, p.806.
40. DORT, L.C., HUSSEIN, J., *J. Otolaryngol.*, **33**, 2004, p.172.
41. SUTHERLAND, K., VANDERVEKEN, O.M., TSUDA, H., MARKLUND, M., GAGNADOUX, F., KUSHIDA, C.A., CISTULLI, P.A., *J. Clin. Sleep Med.*, 10, No .2, 2014, p.215.
42. DOFF, M.H., FINNEMA, K.J., HOEKEMA, A., WIJKSTRA, P.J., DE BONT, L.G., STEGENGA, B., *Clin. Oral Investig.*, **17**, No. 2, 2013, p.475
43. DOFF, M.H., VELDHUIS, S.K., HOEKEMA, A., SLATER, J.J., WIJKSTRA, P.J., de BONT, L.G., STEGENGA, B., *Clin. Oral Investig.*, **16**, No. 3, 2012, p.689.
44. CLARK, G.T., SOHN, J.W., HONG, C.N., *J. Am. Dent. Assoc.*, **131**, No. 6, 2000, p.765.
45. CHECHERITA, L., FORNA, N.C., STAMATIN, O., COBZARU, R, LEON, M.M., CIOLOCA, D., *Rev. Chim. (Bucharest)*, **64**, no. 10, 2013, p. 1172
46. EARAR, K., MATEI, M.N., SANDU, A.V., HRISTIAN, L., BEJINARIU, C., SANDU, I.G., *Mat. Plast.*, **52**, no. 1, 2015, p. 98.
47. CISTULLI, P.A., GOTSPOULOS, H., MARKLUND, M., LOWE, A.A., *Sleep Med. Rev.*, **8**, No.6, 2004, p.443
48. DIELTJENS, M., VANDERVEKEN, O.M., HAMANS, E., VERBRAECKEN, J.A., WOUTERS, K., WILLEMEN, M., De BACKER, W.A., Van de HEYNING, P.H., BRAEM, M.J., *Sleep Breath.*, **17**, No 2, 2013, p.565
49. CHECHERITA, L., FORNA, N.C., MACOVEI SURDU, A., RACOVITA, S., FILIP F., CHIRIAC, A., *Rev. Chim. (Bucharest)*, **64**, No. 11, 2013, p. 1312.
50. ROSU, S., *Mat. Plast.*, **51**, no. 1, 2014, p. 110.
51. CHECHERITA, L., BELDIMAN, M.A., STAMATIN, O., FOIA, L., FORNA, N.C., *Rev. Chim. (Bucharest)*, **64**, no. 8, 2013, p. 864.
52. BORTUN, C.M., ARDELEAN, L., RUSU, L.C., MARCAUTEANU, C., *Rev. Chim. (Bucharest)*, **63**, no. 4, 2012, p. 428.
53. PREJMEREAN, C., MOLDOVAN, M., BRIE, M., FURTOS, G., PRODAN, D., *Rev. Chim. (Bucharest)*, **52**, no. 9, 2001, p. 500.

Manuscript received: 19.05.2014