REZUMATUL TEZEI DE ABILITARE TITLU: MEDICINĂ COMPLEMENTARĂ ȘI ALTERNATIVĂ (MEDICINĂ INTEGRATIVĂ) ÎN DERMATOLOGIE ABSTRACT OF THE HABILITATION THESIS TITLE: COMPLEMENTARY AND ALTERNATIVE (INTEGRATIVE MEDICINE) MEDICINE IN DERMATOLOGY

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This thesis titled "Complementary and alternative (integrative medicine) in dermatology" is divided into five parts, with the first part detailing my scientific contributions after obtaining the doctorate degree. In this part my contributions, as well as results obtained using complementary and alternative medical methods in dermatology are presented. The most frequently used method in the treatment of patients is **homeopathy**, but other therapies such as use of enzymes and phytotherapy (in the case of ulcers) were also utilised and the results demonstrate the positive effects that can be obtained in real, observational practice (Real World Evidence/Data). This approach is becoming increasingly accepted as a valid method of research as not all results obtained from meta-analyses or randomised trials may be applicable in day-to-day clinical practice in all patients.

Homeopathy is a method, which principles were already discussed during the time of Hippocrates. Studies consistently show that it is one of the most frequently used methods of integrative therapy by patients and is recognised by the World Health Organisation WHO. In Romania, the Ministry of Health awards competency certificates in homeopathy to doctors and the Romanian College of Physicians recognises it. Its basic principle "*similia similibus curentur*" is found in conventional medicine. Unfortunately, relative lack of trust amongst the medical corps in homeopathy makes the acquisition of funding for large research, as well as for publication of results difficult, meaning that any results obtained require much more effort than usual. Phytotherapeutic methods were also applied to treat the lower limbs.

The works were published in **ISI** (**JCR**) indexed journals and journals indexed in **International Data Bases.**

In the **second part** of this thesis, my academic activities, which were carried out without being affiliated to a university, are presented. In the **third part** my professional development since graduating from university to the present time is presented, while the **fourth part** shows the directions that I propose, after the defence of this habilitation thesis. The **fifth part** of the thesis contains the bibliography used in the first part of the thesis, as well as the list of my publications in medical journals, following the defence of my doctoral thesis.

Below, I will briefly present some of the studies that contain data and results obtained in treating patients with *complementary and alternative medicine (integrative medicine)*, which are presented in detail in my habilitation thesis.

The first set of case series comprises a study of 32 adolescent patients average age 15.5 years, average duration of disease 2.6 years and equal sex ratio (*Nwabudike LC, CEDH Congress, Prague, 2015*). In this study, **81.25% of patients** went into remission, **3.13% failed treatment and 15.62 were lost to follow up. In the second study,** 83 patients were included, average age 21.5 years, average duration of disease 5.5 years and sex ratio 2:1 (F:M). The results showed that **81.9%** of cases went into remission following treatment, **15.7%** were **lost to follow up**, and **2.4% of cases were treatment failures** (*Nwabudike LC, EADV Congress, Vienna, 2016, Nwabudike LC, Homeopathy, 2021*). A case study (n=2) showed the effect of individualised homeopathic treatment for severe acne. These patients were followed up for long periods of time after cessation of treatment and remained in remission (*Nwabudike LC, Complement Med Res. 2018*).

I studied the effect of homeopathic therapy on verruca vulgaris in a case series and a case study. The case series (*Nwabudike LC*, *EADV Congress, Geneva, 2017*). The case series comprised 8 patients with verruca vulgaris that had not responded to classical treatment for at least 1 year. The sex ratio was 1:7 (F:M), average age was 34.1 years and average duration of verruca was 4.8 years. Co-morbidities included diabetes mellitus, peripheral neuropathy, eyelid cyst, seborrheic dermatitis, psoriasis, and sinusitis. The results showed that **87.5% (7 patients) went into remission**, with an average period to remission of 5.6 months and 50% of co-morbidities remitted. In a case study (n=2), I presented the effect of homeopathy on verruca vulgara. Both cases were females and had type 1 diabetes. With individualised homeopathic treatment, both cases went into remission and had a drop in glycated hemoglobulin level, with a mild increase in C-peptide levels. These results

suggest that individualised homeopathic treatment in vertuca vulgaris could bring about remission of disease, as well as amelioration or healing of co-morbidities.

My research into the effect of homeopathic treatment on psoriasis produced 3 case studies. The first study (Nwabudike LC, Proc Rom Acad, 2011) had 4 patients, aged 14-66 years, F:M ratio was 1:3. The forms of psoriasis were generalised (2 cases), localised -1scalp and 1 nail. Each received an individualised homeopathic treatment and each case had complete and long-lasting remission. The patient with nail psoriasis returned later for a treatment for her daughter who was born after she had gone into remission without relapse for a period of almost 10 years. One patient (14 years old at the time of treatment) with scalp psoriasis later went to university, without a relapse of his psoriasis, according to his mother. Another case study, (Nwabudike LC, Our Dermatol Online, 2017) comprised 3 cases of palmoplantar psoriasis of long duration, all treated with homeopathy. There were 2F and 1M patients aged 55-66 years with a duration of psoriasis up to 30 years in one case. Each patient received individualised homeopathic treatment and went into remission. The results suggest that homeopathy may be useful in bringing about long-term remission of psoriasis. Finally, in a recent case study of mine (n=2), the first patient was a male, aged 56 years with a 17year history of psoriasis, presented with erythroderma and received an individualised homeopathic treatment, with complete amelioration of the cutaneous lesions, as well as the nail lesions. The second patient was a 32-year-old patient with lesions of psoriasis vulgaris and inverse psoriasis (in the inguinogenital area). She was treated with individualised homeopathy and the lesions remitted. (Nwabudike LC, Am J. Homeopathic Medicine, 2020). It should be noted that this patient became pregnant during the first few months of homeopathic treatment and did not need to stop therapy. These 3 studies demonstrated the effect of homeopathy in the long term for the therapy of psoriasis and that it can be used during pregnancy, without teratogenic effects.

The effect of homeopathy in lichen planus were presented in a case study, which comprised 4 patients (*Nwabudike LC*, *Miulescu M*, *Tatu AL*, *Exp Ther Med*, 2019). There were 2 females and 2 males aged between 41 and 65 years, with disease duration from 7 months – 27 years. All patients had a generalised form of the disease and 2 patients had mucosal involvement. All were treated with individualised homeopathy and went into remission. One patient suffered from anosmia, which improved with the same individualised homeopathic treatment for lichen planus. The same patient returned 3 years later, requesting treatment for his child. He was still in remission and these last photographs have been included in the habilitation thesis. The results suggest that individualised homeopathy may

be useful in the treatment of generalised lichen planus of long duration, as well as for mucosal lichen planus, with long term remissions.

I published a case study on the effects of individualised homeopathy in the treatment of mycosis fungoides (*Nwabudike LC*, *J. Am Acad Dermatol, 2017; Nwabudike LC*, *Homeopathy, 2019*). The study comprised 3 patients aged between 22 and 84 years, with mycosis fungoides confirmed by immunohistochemistry. Each patient received an individualised homeopathic medicine, after which he went into remission. These results indicate the possibility because mycosis fungoides does not spontaneously remit.

Recurrent urinary tract infections are an important and frequently encountered problem. I published a case study with 3 patients, all female, with relapsing urinary tract infections (*Nwabudike LC*, *Proc Rom Acad*, 2017). Their ages were between 4 months and 54 years. All were culture positive and, following homeopathic treatment, became culture negative. Two cases had *E coli* and on case had *Klebsiella spp*. The results suggest that homeopathy could be useful in the treatment of recurrent urinary tract infection, thereby sparing the use of antibiotics, especially in the very young, as the side effects of antibiotics could constitute a serious problem.

Rosacea is a frequently encountered cutaneous disorder. It can be a significant cause of diminished quality of life. I published a case study comprising 3 patients with rosacea aged 32-53 years (*Nwabudike LC, Proc Rom Acad, 2012*). Of these, two were female. Each patient received individualised homeopathic medicine and all went into remission, without relapsing. This suggests that homeopathy may contribute to the remission of rosacea.

I published a case study of atopic dermatitis comprising three patients, aged 10 months to 22 years (*Nwabudike LC, Our Dermatol Online, 2012*). Two patients were female (aged 10 months and 22 years) and the other (11 months of age) was male. They each received individualized homeopathic treatment and emollients. The patients remitted and remained in remission. Homeopathy proved to be useful in the treatment of atopic dermatitis, thereby suggesting it could be a steroid sparing treatment. Another case study was presented in the chapter written by me s sole author - *Homeopathy in the Therapy of Acne and Rosacea*. In: Rupani R.N., Lio P.A. (eds) *Integrative Dermatology*. **Springer, Cham**., 2021. The case was of a patient with a 3-year history of facial rash, which manifested as erythema, oedema and facial dryness, without ocular involvement. Clinically, the patient had facial erythema and enema, with papules and pustules. She was treated with the homeopathic medicine *Platinum* metallicum, at MK potency. At 6 weeks, the patient was already improved, with

few new lesions. After 5 months, she was almost without lesions and remained in remission at a follow up visit, which took place 15 months after the onset of treatment.

With regard to atopic dermatitis, I published a case study of 3 patients, aged 10 months to 22 years (*Nwabudike LC, Our Dermatol Online, 2012*). Two patients were female (10 months and 22 years of age) and the other (11 months of age), was male. They received individualised homeopathic medicines and emollients. The patients went into remission and remained in remission. Homeopathy proved to be useful in the treatment of atopic dermatitis, which could then eliminate or diminish the need for steroid treatment, thereby becoming a "steroid-sparing" agent.

Another case study comprising 2 females, 25 and 42 years old with severe, longstanding seborrheic dermatitis (*Nwabudike LC, Our Dermatol Online, 2011*) and treated with individualised homeopathy was published by me. The patients went into remission, showing the potential of homeopathy in the treatment of longstanding seborrheic dermatitis.

I showed the potential of homeopathy to produce remission in the treatment of dermatitis herpetiformis (*Nwabudike LC, Homeopathic Links, 2015*) in a case treated with individualised homeopathy. This case was followed up for a period of several years after the patient went into remission. Neither the cutaneous lesions, nor the intestinal derangements remitted. The patient was able to feed without being on a special diet.

Individualised homeopathy was used for a case of melasma (*Nwabudike LC*, *Homeopathic Links*, 2012), which went into remission and remained that way following an annual follow up.

I recently published a case study in which the homeopathic medicine *Apocynum cannabinum*, combined with furosemide at a dose of 120mg/day was successfully used in the treatment of a patient with elephantiasis nostras verrucosa. It will be recalled that this disorder does not spontaneously remit and diuretics such as furosemide are not very useful, due to their lack of efficacy in such situations (*Nwabudike LC et al., Exp. Ther. Med., 2022*)

Cutaneous ulcers are a major health problem. They are frequently encountered, requiring huge costs and time for their therapy. A multidisciplinary team is required for the therapy of this kind of ulcer. Their differential diagnoses are vast and includes malignant ulcers. I have documented two cases – one case of squamous cell carcinoma at the level of the plantar area, suggesting a neuropathic ulcer and which was treated as such for 3 years in other clinics (*Nwabudike LC*, Gutu D, *Clin Exp Dermatol, 2021*). The second was a case of malignant melanoma at the level of the heel of a patient with diabetes, treated also for several

years as a case of diabetic ulcer. Biopsy demonstrated that this lesion was a melanoma (*Nwabudike LC*, et al. *Clin Cosmet Investig Dermatol*, 2022). Lack of multidisciplinary collaboration contributed, possibly, to the long term, non-corresponding therapy and these cases teach us that an ulcer at the level of the foot of a patient with diabetes, which does not respond to therapy within a reasonable time should be evaluated for other differential diagnoses.

Naturopathic therapies are useful in the management of cutaneous ulcers. I presented several case studies, which showed the effect of Miculicz ointmenent – containing balsam of Peru - (*Nwabudike LC, Tatu AL, Am J Ther 2018*) and the effect of bee honey on ulcers (*Nwabudike LC, Maruhashi E, Wounds Int 2017; Nwabudike LC, Maruhashi E, Wounds Middle East 2017; Nwabudike LC, Maruhashi E, EWMA Congress, 2018*).

Using Miculicz ointment, which contains balsam of Peru, it was possible to heal a chronic ulcer, which had been present for 6 months prior to presentation, on the foot of a 50-year-old male patient with type 2 diabetes and severe arteriopathy, thereby avoiding amputation. The treatment was applied daily by the patient and the patient's progress was monitored at my office (*Nwabudike LC*, *Tatu AL*, *Am J Ther. 2018*).

Bee honey was used by us in the treatment of foot ulcers of patients with diabetes mellitus. The first case was of a patient aged 85 years, with type 2 diabetes, renal insufficiency, ischemic cardiomyopathy and an ulcer on the anterior surface of the right leg. The ulcer healed over a period of 3 weeks (*Nwabudike LC, Maruhashi E, Wounds Int. 2017*; *Nwabudike LC, Maruhashi E, Wounds Middle East, 2017*). This work was published in the journal *Wounds International* and, at the request of the Publishers, republished in *Wounds Middle East.*

I also used bee honey in the treatment of a post amputation ulcer in a noncompliant patient. The patient refused conventional antidiabetic therapy, preferring to use antidiabetics of plant origin and from other sources, he rejected the recommendation to do a glycated haemoglobin test and was not dressing his wounds adequately. Despite his noncompliance, the patient responded well to a topical therapy with bee honey (*Nwabudike LC, Maruhashi E EWMA, Krakow, 2018*).

The Koebner phenomenon – the isomorphic phenomenon – is very well known in dermatology as a clinical diagnostic sign. There are classic forms of Koebner (seen with vitiligo, lichen planus and psoriasis); pseudo-Koebner from seeding (verruca vulgara, molluscum contagiosum); forms with well documented, occasional lesions (Behcet disease and pyoderma gangrenosum) and, finally, forms with rare association (pemphigus, lichen

nitidus). The Wolf phenomenon is considered an isotopic phenomenon, in which the disease appears where an older disease has been healed. We discussed both phenomena through their mechanisms and mod of appearance and argued the case for them not to be considered separate entities, but for the Wolf phenomenon to be considered a fifth form of Koebner (*Nwabudike LC, Tatu AL, J Eur Acad Dermatol Venereol, 2018*).

In the form of Koebner that has been rarely mentioned – type IV – I published a case, which has never been published in the literature. This was about a case of Koebner phenomenon in a patient with pityriasis rosea. The lesions appeared at the sites of venepuncture, at the level of the cubital fossae, together with classic lesions of pityriasis rosea (*Nwabudike LC, Our Dermatol Online, 2013*).

The inflammatory response to the SARS-CoV-2 virus, as well as the increase in levels of cytokines could be the basis of the vesicular rash, as well as of the Koebner phenomenon occurring especially in type V Koebner (Tatu AL [....] *Nwabudike LC*, *Clin. Cosmet Investig Dermatol, 2021; Tatu AL, Nadasdy T, Nwabudike LC, J Eur Acad Dermatol Venereol, 2021*).

Field cancerization is a phenomenon that was initially described in 1953 by Slaughter. It refers to the possibility of producing a tumour in an area of immunosuppression. We hypothesized on the existence of a generalized field cancerization to explain the possibility of occurrence of tumours far from the primary tumour, without these being metastases. (*Nwabudike LC, Tatu AL, J. Eur Acad Dermatol Venereol, 2018*). We also speculated that field cancerisation could be caused by medications not usually associated with immunosuppression, such as tetracyclines (*Nwabudike LC, Tatu AL, J. Eur Acad Dermatol Venereol, 2018*), hydrochlorothiazides (*Tatu AL, Ciobotaru OR, Miulescu M, Buzia OD, Elisei AH, Mardarea N, Diaconu C, Robu S, Nwabudike LC, Rev Chim, 2018*) and statins (*Nwabudike LC, et al. Rev Chim, 2018*). Thus, we tried to show that the increased rate of cancer could originate also in treatments used for other disorders. This is still being discussed today.

In the second part, I discussed my areas of interest, which include integrative dermatology (complementary and alternative medicine in dermatology), diabetic foot ulcers, as well as the history and philosophy of dermatology and medicine, in general.

I presently have a **Hirsch score of 13 (ISI)** and a cumulative impact factor as principal author of **23.985**.

I began to write book chapters connected with these topics before the finalisation of my doctorate thesis and continued afterwards. The chapters written after the finalisation of my doctoral thesis are *A Tale of Diabetic Neuropathy* (in the book *Istoria neuropatiei diabetice în România*, 2013, C. Ionescu-Tîrgoviste, [ed.]), in which I outlined the history of Romanian research in the field of diabetic neuropathy, including my own contributions. In the chapter *Diabetic Foot Ulcers* (Diabetic Complications. New Insights and Solutions, 2014, Cheta D, [ed]) I discussed the up-to-date data connected with the aetiology, pathology and treatment of this disorder, including my own experience in the field.

Some chapters written, in collaboration with other colleagues, focussed on malignant melanoma and include -

F.C. Bujoreanu, D.S. Radaschin, L.C. Nwabudike, A.L. Tatu Cutaneous melanoma from the anterior thorax: a case report (in Clinical Cases in Melanoma Lotti, Torello; Tirant, Michael; Wollina, Uwe 2020, (Eds.). Springer Nature Publishers ISBN 978-3-030-50820-3
L.C. Nwabudike, A.L. Tatu, A.M. Oproiu, M. Costache When Dermoscopy exonerates a suspect and "indicts" another lesion (in Clinical Cases in Melanoma Lotti, Torello; Tirant, Michael; Wollina, Uwe 2020, (Eds.). Springer Nature Publishers ISBN 978-3-030-50820-3

Other chapters are related to pigmentary disorders and include -

A.L. Tatu, D.S. Radaschin, F.C. Bujoreanu, L.C. Nwabudike. *Homogeneous black, pigmented lesion of the fifth toe* (in *Clinical Cases in Pigmentary Disorders* Lotti, Torello; Tirant, Michael; Parsad, Davinder 2020, (Eds.). Springer Nature Publishers ISBN 978-3-030-50823-4

L.C. Nwabudike, A.L. Tatu, D.S. Radaschin, V Ardeleanu *The dermatologist's fingernail* in Clinical Cases (in *Clinical Cases in Pigmentary Disorders* Lotti, Torello; Tirant, Michael; Parsad, Davinder 2020, (Eds.). Springer Nature Publishers ISBN 978-3-030-50823-4

There were other chapters, which focussed on homeopathy including -

L.C. Nwabudike, A.L. Tatu. *Dark facial spots and a rash* (in *Clinical Cases in Pigmentary Disorders* Lotti, Torello; Tirant, Michael; Parsad, Davinder 2020, (Eds.). Springer Nature Publishers ISBN 978-3-030-50823-4

L.C. Nwabudike *Homeopathy in the Therapy of Acne and Rosacea.* (in *Integrative Dermatology*, Rupani R.N., Lio P.A. 2021, (eds). Springer, Cham.

I have taught at competency courses in homeopathy, which were organised by UMF Iaşi and the Ministry of Health.

I have been a Speaker at multiple international and national conferences, where I presented papers in the field of complementary and alternative medicine (integrative medicine), such as Beijing, 2009; Paris 2018; Madrid 2019; Barcelona 2019; as well as nationally at the conferences of the Romanian Society of Dermatology (2017, 2019).

I was Guest Editor for the journals Dermatologic Therapy (impact factor 2.851)

I have been a Peer Reviewer for the following journals (verifiable on Publons) Alternative Therapies in Health and Medicine, Diagnostics, Journal of Integrative Medicine, Homeopathy, Clinical and Experimental Dermatology, Dermatologic Therapy, International Journal of Dermatology, Children, Atmosphere, Biomedicines, Clinical, Cosmetic and Investigational Dermatology.

I am a member of the board of the international journal Our Dermatology Online (<u>www.odermatol.com</u>), since 2011.

I am a member of faculty for the 5-CC (5-Continent Congress), and in this role, I presented many articles including a course (Residents and Fellows Symposium, 2019), in which I taught on homeopathy and its role in the treatment of dermatologic disorders.

All these show my ability, either alone, leading or being part of a research team to carry out research, which culminated in scientific publications that are accepted and internationally recognised. They also show my ability to work in a teaching role.

In the third part, I detailed my professional development from graduating at the University of Lagos (**MBBS**, 1989), to postings in dermatology at the Colentina Hospital (1992-1995). During this period, I also underwent the competency courses in acupuncture and homeopathy (both in 1995). In 1998 I passed the American Licensure exam (USMLE/ECFMG)

In 2007 I became Doctor in Medicine, while in 2009 I became Senior specialist (medic primar). In 2012 I graduated the course for trainers in acupuncture of the Ministry of Health and in 2017 I passed the exams of the Royal College of Physicians (UK) in general internal medicine, thereby becoming elected to the title of MRCP(UK).

I am, at present, a member of the Romanian Society of Dermatology (SRD), the Romanian Association of Clinical Homeopathy (ARHC), American Academy of Dermatology (AAD), European Academy of Dermatology and Venereology (EADV), Royal College of Physicians (RCP) and Secretary (current President-elect) of the European Society for the History of Dermatology and Venereology (ESHDV).

I am licenced to practice medicine by the Romanian College of Physicians, The Bucharest College of Physicians, The General Medical Council (UK) and the Nigerian Medical Council (Nigeria).

In the third part of my thesis, I elaborated on my personal desire to continue my research in the directions that I have already begun to work in. Thus, I will continue to publish and carry out research into the fields of complementary and alternative medicine (integrative medicine) in dermatology, into the field of diabetic foot ulcers, with the hope of contributing to the diminution of the number of lower limb amputations, as well as into the history and philosophy of medicine, which will allow us to look into the past to prepare for the future.

In the fifth part I presented the bibliography, which I used in the elaboration of the first part of my habilitation thesis. In this part I also one can find the list of papers published by me – in **ISI and other International Data Bases** -, published by me after obtaining the title of Doctor of Medicine.

I hope to have the opportunity to direct doctoral theses in the fields that I have mentioned in order to contribute to the training of new generations of physicians who might continue this work, thereby taking it to even greater heights. I also hope to be given the chance to teach new generations of doctors and students, who will have a new attitude and approach, which would be much more open to these fields, thus easing the general public's access to them. Finally, I would like to use the reputation that I have already garnered in the press, as well as the possibilities that the Habilitation offers to promote integrative medicine, the correct approach to diabetic foot ulcers, as well as the philosophy and history of medicine.