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Research Article

A novel topical phytotherapy for normalization of aberrant leg-anatomical and biochemical risks in failed spine surgery associated with knee-osteoarthritis: A unique case study

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ABSTRACT

Objective: The aim of the study was to normalize the aberrant leg-anatomical and biochemical parameters, to relieve pain syndromes and to improve quality of life without revision of failed spine surgery (FSS) and surgical intervention of coexisted knee-osteoarthritis (KOA) correlated with radiological images by specialized topical phytotherapy.

Methods: A 45-year-old gentleman was advice to undergo revision of FSS and surgical intervention for KOA. He refused to do the further surgeries and treated in OPTM Health Care during January-February 2018. Anatomical measurements included bilateral: the gap at the knee joint between the short head of the biceps femoris and the level of the bed in supine, diameters of muscles at the thigh, the calf, 4cm above and below the patella, angles of straight leg raising, knee flexion, and extension in supine, and biomarkers (Interleukin-10, Tumour necrosis factoralpha, C-reactive protein, Creatine kinase-muscle, and Aldolase-A) were measured pre- and post-treatment using appropriate protocols. The patient was treated for 12-week with phytoextracts of previously established seven medicinal plants.

Results: The percentages of improvements for all the above-mentioned abnormal leg-anatomical and biochemical parameters were observed at post-treatment: 63.81, 2.28, 0.81, 5.22, 0.82, 160.00,73.75 and 50.00 respectively for right leg and 69.60, 5.79, 2.79, 9.93, 0.82, 290.00, 85.33 and 54.55 for left leg in case of leg-anatomical features and 87.72, 66.39, 77.27, 22.77 and 48.41 respectively for biomarkers and that for international acclaimed pain parameters under VAS, WOMAC, ODI, LEFS, KPS and BMI were highlighted in the earlier study and the same under KOOS were recorded as pain (86.11), symptoms (89.29), ADL (79.42), Sport & Recreation (75.00), and QOL (68.75) with improved radiological images both lumbar and knee-joints as assessed by KL-grading scales(≥ 2).

Conclusion: Results showed the deranged leg-anatomical and biochemical risks, together with impaired international pain parameters during FSS associated with KOA can be normalized by specialized topical phytotherapeutic treatment within 12-week.

Keywords: Failed spine surgery; Phytotherapy; Medicinal plants; Alternative treatment for FSS; Biomarkers.

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INTRODUCTION

Lumbar spine surgery (LSS) is undertaken, when all possible pharmaco- and physical therapies failed, for lumbar herniated disc (LHD) also termed as lumbar slipped disc (LSD) due to compression between the two vertebrae L_4 and L_5 or L_5 and S_1 or other for multiple vertebral compressions of two or more vertebrae, usually L_3 - L_4 , L_4 - L_5 and L_5 - S_1 , known as lumbar spondylosis (LS). LHD or LS emphasized intervertebral disc(s) degeneration in the lumbar region, resulting which the nearby nerve roots and cauda equina are impinged and stimulated by the nucleus pulposus slipped out through a crack in the annulus fibrosus of a disc, causes severe pain, numbness, weakness in the lower limbs or paralysis or loss of bowel and bladder control or sexual dysfunction and finally leads to disability. But the mystery remained silent that along with the compression of lumbar-

disc(s), the degenerative changes also occur simultaneously on the knee-joint(s) commonly known as knee-osteoarthritis (KOA). The KOA has been characterised by the potential loss of joint cartilage as well as osteophyte formation, connective tissue damage, pain symptoms, joint effusion, restricted movement of joints, tenderness and crepitus in the joints.¹⁻⁶ The goals of a lumbar fusion surgery are to un-pinch or decompress nerves as well as to intentionally eliminate one or more painful joints.

The author had already emphasised in the previous studies that the degenerative changes in lumbar region always occur simultaneously with osteoarthritic changes in the bilateral knee-joints and vice-versa. Therefore, the status of degeneration cannot always be judged by measuring the parameters of sensation of pain.⁷ Nevertheless, the author had further established that these disorders can be the

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normalized by topical application of specialized phytoconstituents possible cartilage regeneration.⁸

However, it has been observed that revision of LSS requires in most patients due to infection, obesity, physical activity, or such other reasons. Among many surgical procedures, Lumbar Spine Fusion Surgery (LSFS) is a common treatment method to relieve pain and provide quality of life worldwide.9 Moreover, during failed LSS, various abnormal leg-anatomical and other features were observed such as, muscular wasting and strength, unable to rise the legs while lying on bed or walking, unable to fold the knee joints and such other complications. 10 Besides these, other biochemical risk factors develop in the serum of patients such as abnormal levels of Interleukin-10 (IL-10), Tumour necrosis factor-alpha (TNF-α), C-reactive protein (CRP), Creatine kinase-muscle (CK-MM), and Aldolase A (Aldo A) along with inflammation, obesity, severe pain radiating to lower limbs, numbness, and severe disability of performing daily activities also persist.

Furthermore, the author had already established earlier that abnormal muscle morphology and musculo-postural features of the legs and abnormal biochemical features, and imaging markers are suitable diagnostic protocol for the detection of early progression and risk of LHD and KOA and established the treatments with the help of phytotherapeutic method for LHD and KOA.¹¹⁻¹⁴

The present case study was aimed to normalize the deranged anatomical features such as bilateral gap of knees between the point of short head of the biceps femoris at the lateral knee joint and the surface of the bed while supine (KGB), bilateral diameters of the thigh muscles (DTM), calf muscles (DCM), 4cm above the patella (DAP) and below the patella (DBP), bilateral straight leg raising (SLR), the angles of kneeflexion in supine (KFS), and knee-extension in supine (KES), which become asymmetrical between the right and left legs due to damage of various connective muscles and tissues during FSS associated with KOA as per established protocol developed by Ganguly.15 Further to normalize the aberrant levels of biochemical parameters such as Tumour necrosis factor-alpha (TNF- α), a pro-inflammatory cytokine, increases during inflammation in musculoskeletal disorders and acts as an autocrine stimulator and paracrine inducer of other inflammatory cytokines such as Interleukin-10 (IL-10), an anti-inflammatory cytokine, decreases. The study of these two biomarkers are suitable to detect the rate of inflammation and the progression of musculoskeletal disorders because TNF- α and IL-10 in blood showed antagonistic mechanism, C-reactive protein (CRP) levels increase caused by inflammation, 16-17 Creatine kinase-muscle (CK-MM) levels elevated due to muscular dystrophy, connective tissue damage, etc. 18-19 and Aldolase A (Aldo A) levels increase because of skeletal muscle damages and bone erosion.²⁰ In addition, to improve daily physical functional abilities as per international acclaimed pain parameters such as Visual Analogue Scale (VAS),21 The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC),22 Oswestry Disability Index (ODI),23 Lower Extremity Functional Scale (LEFS),24 Karnofsky Performance Scale (KPS),25 Body Mass Index (BMI),26 and Knee-injury and Osteoarthritis Outcome Scale (KOOS)27 without revision of FSS and any surgical intervention for KOA, which developed simultaneously, correlated with radiological images for lower lumbar spine and knee-joints as assessed by the Kellgren-Lawrence (KL)28 grading systems with the help of specialized topical phytotherapeutic treatment protocol for 12 weeks, not yet been attempted so far.

Therefore, the present study has portent novelty concepts for the treatment of both FSS and associated KOA thereon,

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into the categories of relevant neuro-muscular- lower leganatomical features, the specific biochemical markers, and the international approved pain parameters.

CASE STUDY

A 45-year-old man was suffering with severe pain radiating to lower limbs, weakness, inflammation and stiffness on both the knee joints, massive muscular wasting in the thigh and calf regions, unable to raise their legs while supine, prone and standing positions, impaired function, and limitations of daily activities after LSS had undergone 3 years back and was in the wheelchair. He was advised to further revision of LSS along with some surgical intervention to his knee-joints. But he has refused to undergo further surgeries and came to OPTM Health Care (P) Ltd, India, for treatment during the period January-February 2018. The study protocol was evaluated and approved by the OPTM Research Institute Ethics Committee. An institutional review board-approved consent form for physical examinations, blood sample collections and lumbar spine as well as bilateral knee-joint images (X-rays) required for the study was signed by the patient. Baseline demographic characteristics of the patient was shown in the previous study by Ganguly A³⁸. The physical examinations were made at the baseline and at the end of 12 weeks of post-treatment including anatomical measurements such as KGB, DTM, DCM, DAP, DBP, SLR, KFS, and KES (Figures 1-2).

A meter scale was used to measure KGB. The measurements of DAP, DBP, DTM and DCM were performed using a meter tape and a goniometer was used for straight leg raising, flexion and extension measurements in accordance with the American Academy of Orthopedic Surgeons (AAOS).²⁹ The methods of anatomical measurements had already elaborated in the earlier studies.^{8,12,30-32}

Evaluation of risk factors such as inflammation, muscle degeneration, bone erosion, and skeletal muscle diseases were recorded through the estimation of biomarkers, IL-10, TNF- α , CRP, CK-MM, and Aldo A levels at the pre- and post-treatment of 12-week using appropriate kits and protocols.8,12,30-32 The results of the biomarkers at pre- and post-treatment are shown in Figures 3-5.

The author had already elaborated in details the treatment protocol based on the aims, principles and theories, accessories and mode of stimuli used in the therapy, effects of chemical, mechanical, thermal and electrical stimuli used in the treatment protocol, the specific programmed postural positions for the regimentation of neuromuscular strength required in the therapy and period of treatment for 12 weeks with necessary documentation in the previous studies.8,12,30-

The graphical representations of percentages improvements on pain, stiffness, physical function and quality of life and body weight under VAS, WOMAC, ODI, LEFS, KPS and BMI had already been elaborated in connection with the patient in the earlier study by Ganguly A³⁸. The results of pre-and post-treatment and the percentages of improvements after the phytotherapy for 12week under KOOS (Figures 6-7), anatomical features for the patient such as KGB, DTM, DCM, DAP, DBP, SLR, KFS, and KES are exhibited in Figures 1-2 & 8-9. The same for the biochemical markers such as IL-10, TNF-α, CRP, CK-MM and Aldolase A at pre- and post-treatment and their percentages of improvements are shown in Figures 3-5 & 10-12. The patient was not being treated by oral medications; injections; massage with any type of herbal gels; and any type of alternative treatments such as homeopathic, ayurvedic, herbal or such others for diminishing pain or inflammation, for muscle relaxation, or to improve the skeletal muscles

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four weeks prior to post-treatment of 12 weeks. The Kellgren- Lawrence (KL) grading system of radiographic lumbar spine and knee-joints of the patient at post-treatment were evaluated for bone erosion, reduction of the gap between the lower vertebrae, the femoral and tibial

compartments, Varus deformities was recorded as ≥ 2 . The radiological images of lumbar spine and both knee-joints of the patient were evaluated at pre- and post-treatment in the present study and depicted in Figures 13-14.

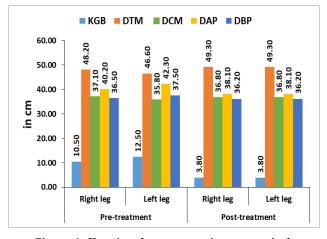


Figure 1: Showing the comparative anatomical parameters of KGB, DTM, DCM, DAP & DBP at pre- & post-treatment

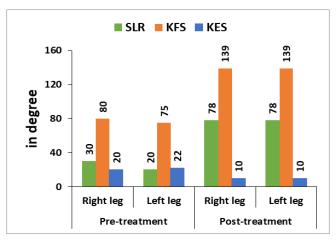


Figure 2: Showing the comparative anatomical parameters of SLR, KFS & KES at pre- & post-treatment

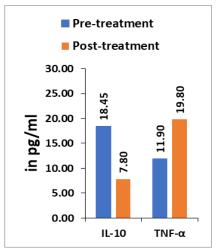


Figure 3: Showing the comparative biomarkers of IL-10 TNF- α at pre- & post-treatment

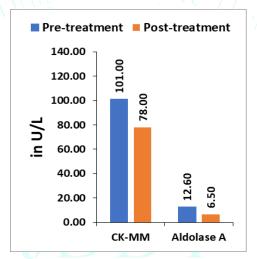


Figure 4: Showing the comparative biomarkers of CK-MM & Aldolase A at pre-& post-treatment

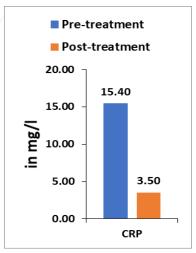


Figure 5: Showing the comparative biomarker of CRP at pre- & post-treatment

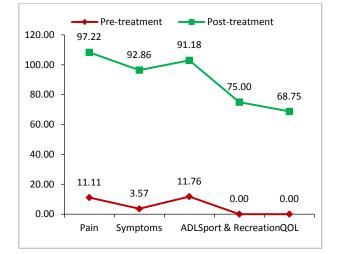


Figure 6: Showing the comparative KOOS Parameters at pre- & post-treatment

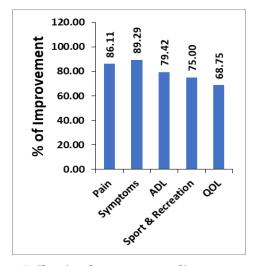


Figure 7: Showing the percentage of improvement of comparative KOOS Parameters at post-treatment

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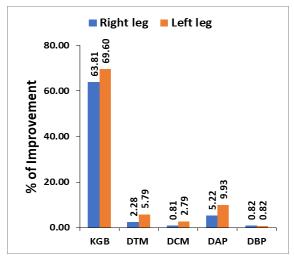


Figure 8: Showing the percentage of improvement of anatomical parameters of KGB, DTM, DCM, DAP & DBP at post-treatment

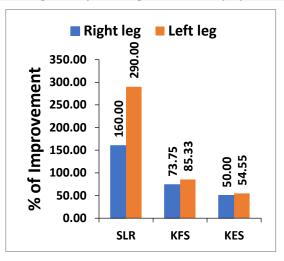


Figure 9: Showing the percentage of improvement of anatomical parameters of SLR, KFS & KES at post-treatment

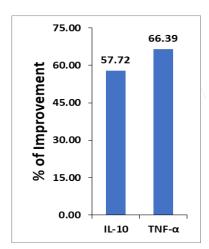


Figure 10: Showing the percentage of improvement of biomarkers of IL-10 & TNF- α at post-treatment

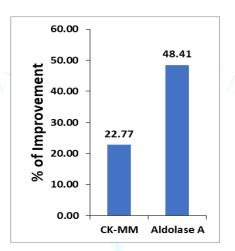


Figure 11: Showing the percentage of improvement of biomarkers of CK-MM & Aldolase A at post-treatment

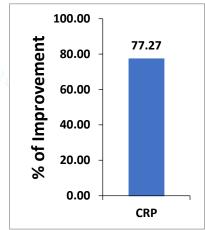
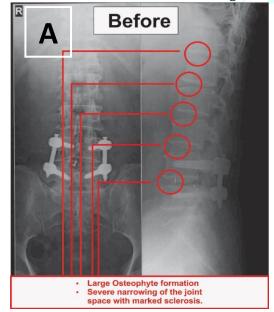


Figure 12: Showing the percentage of improvement of biomarker of CRP at post-treatment

Age: 45 Years, Sex: Male



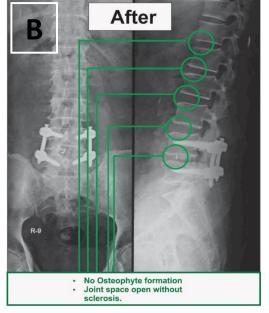
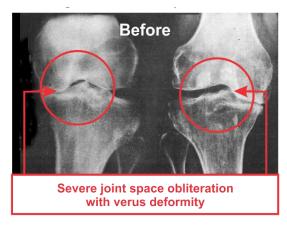


Figure 13: Radiographic images of before and after the treatment of lumbar spine

[Source: Ganguly A, Ganguly D, A novel approach for failed lumbar spine surgery with topical phytotherapeutic treatment: a unique case study, Journal of Drug Delivery & Therapeutics, 2018; 8(6-s):135-140]

Age: 45 Years, Sex: Male



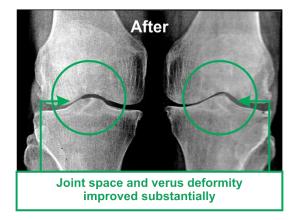


Figure 14: Radiographic images of before and after the treatment of knee joints

DISCUSSION

The main purpose of LSS and surgical intervention in knee-joints is to reduce the chronic pain, increase the functional abilities thus to improve quality of life. But the relevant risk factors associated with LSS are medical complications such as pneumonia, heart attack, stoke and blood clots in the legs and surgical complications include infection, bleeding, nerve injury, spinal fluid leak, injury to the arteries and veins and injury to the intestines or the urinary system. Moreover, when the bone across one or more joints does not fully heal resulting which the stabilizing hardware and cages can loosen or even break, the revision of LSS is required. The patients at risk for poor bone healing include smokers, diabetic and individuals with poor bone health and thus the revision of FSS associated with KOA is very risky, complicated, low success rate and expensive.³³⁻³⁷

Several researchers had already reported the medicinal effects on pain, inflammation and stiffness of muscles on human body of the phytochemicals contained in *Cissus quadrangularis* (whole plant), *Rosemarinus officinals* (leaves and flowers), *Calotropis gigantea* (root and leaves), *Zingiber officinalis* (rhizome), *Boswellia serrata* (resin), *Curcuma longa* (rhizome), *Withania somnifera* (root) and *Sesamum indicum* (seeds), and their mechanism of actions.^{8,12,45} This phytotherapeutic treatment may have synergistic effect of the phytochemicals used in the therapy.

It has attempted earlier that the topical application of phytoconstituents from the extracts of aforesaid seven Indian medicinal plants mixed with virgin sesame oil and beeswax is extremely useful for the treatment of musculoskeletal diseases like slipped disc, KOA etc. In the present treatment protocol, the extracts of above-mentioned seven medicinal plants have been used, which has discussed in earlier studies.³⁸ But no one has not been reported before that biochemical markers such as IL-10, TNF-α, CRP, CK-MM and Aldo A can be within their normal ranges (Figures 3-5) after the topical application of phytoconstiuents from abovementioned medicinal plants along with normalization of anatomical derangement (Figures 1-2), pain, stiffness and physical functional activities under various international acclaimed pain parameters such as VAS, WOMAC, ODI, LEFS, BMI and KOOS (Figure 6) supported by radiographic changes as assessed by K-L grading scales (from ≥ 4 to ≥ 2) after LSS associated with KOA (Figures 13-14). $^{39-45}$

It is interesting to note that the measurements of bilateral KGB, DAP, DBP and KES, were widely and asymmetrically increased, and the bilateral DTM, DCM, SLR, and KFS, were

widely and asymmetrically decreased at the baseline because of cumulative effects of muscle wasting, and diminished strength of various connective muscles and tissues during LSS together with KOA and they were almost symmetrical after the treatment of 12-week (Figures 1-2).^{7,12,15,30-31}

Moreover, in the ealier studies, the author had already shown no need of TKR, revision of TKR, surgery for LHD and normalization of aberrant leg-anatomical parameters and non-standard levels of biomarkers such as IL-10, TNF- α , CRP, CK-MM and Aldo A developed during musculoskeletal disorders in lumbar region and knee-joints in patients with the help of topical phytotherapy treatment. 11,13-14

CONCLUSION

From the results and discussion, it is firmly concluded that the risks of deranged leg-anatomical features such as KGB, DTM, DCM, DAP, DBP, SLR, KFS and KES and aberrant levels of biomarkers include IL-10, TNF- α , CRP, CK-MM and Aldo A, impaired international acclaimed pain parameters including quality of life as assessed by VAS, WOMAC, KPS, ODI. LEFS, BMI and KOOS and imaging markers for lower lumbar spine and knee-joints developed during failed spine surgery associated with KOA can be normalized with the help of specialized topical phytotherapeutic treatment protocol within 12 weeks. Further researches should be undertaken on phytochemicals characterization by using Mass Spectroscopy.

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Conflicts of interest

The author declares that there are no conflicts of interest regarding the present study.

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REFERENCES

- Felson DT, Epidemiology of hip and knee osteoarthritis, Epidemiol Rev, 1988; 10:1-28.
- Bijlsma JW, Berenbaum F, Lafeber FP, Osteoarthritis: an update with relevance for clinical practice, Lancet, 2011; 377:2115-2126.
- Johnson VL, Hunter DJ, The epidemiology of osteoarthritis, Best Pract Res Clin Rheumatol, 2014; 28:5-15.
- Mabey T, Honsawek S, Role of vitamin D in osteoarthritis: Molecular, cellular, and clinical perspectives, Int J Endocrinol, 2015; 2015: (http://dx.doi.org/10.1155/2015/383918).
- Li H, Zeng C, Wei J, et al. Serum calcium concentration is inversely associated with radiographic knee osteoarthritis: A crosssectional study, Medicine, 2016; 95(6).
- (DOI: 10.1097/MD.0000000000002838).
- Slemenda C, Heilman DK, Brandt KD, et al. Reduced quadriceps strength relative to body weight: a risk factor for knee osteoarthritis in women, Arthritis Rheum, 1998; 41(11):1951-1959.
- Ganguly A, The degenerative changes in lumbar region always lead to bilateral degenerative changes in knee-joints and vice versa: Sensation of pain cannot only be the parameter of degeneration, Anat Physiol, 2015; S3:002doi:10.4172/2161-0940.S4-005.
- Ganguly A, Degenerative changes in lumbar-region occur simultaneously with bilateral-osteoarthritic changes in kneejoints and vice-versa: Normalisation with topical application of phytoconstituents by specialized techniques involving possible cartilage-regeneration, International Journal of Recent Scientific Research, 2015; 6(9):6331-6346.
- 9. Weinstein JN, Lurie JD, Olson PR, Bronner KK, Fisher ES, United States' trends and regional variations in lumbar spine surgery: 1992-2003, Spine (Phila Pa 1976), 2006; 31(23):2707-14.
- Pengel LH, Herbert RD, Maher CG, Refshauge KM, Acute low back pain: systematic review of its prognosis, BMJ, 2003; 327(7410):323.
- Ganguly A, Ganguly D, Aberrant biomarkers, leg anatomy and pain parameters are the risk factors in lumbar-herniated disc: A novel diagnostic protocol. J Orthopedics Rheumatol, 2018; 5(2):1.
- Ganguly A, Diagnosis of knee osteoarthritis risk through abnormal musculo-postural features, Int Arch BioMed Clin Res, 2018; 4(1):1-4.
- 13. Ganguly A, Ganguly D, Evidence-based tropical phytotherapeutic treatment protocol for lumbar slipped disc: An approach with biochemical, anatomical, functional disability and radiological parameters, IOSR Journal of Dental and Medical Sciences, 2018; 17(9):01-20.
- Ganguly A, Ganguly D, Banerjee SK, Topical phytotherapeutic treatment: Management of normalization of elevated levels of biochemical parameter during osteoarthritic disorders: A prospective study, J Orthopedics Rheumatol, 2018; 5(1):14.
- Ganguly A, Diagnosis, prevention & phytotherapy for osteoarthritic disorders: pain diagnostic parameters and prevention of OADs. Scholars press, UK: 2017.
- Thompson D, Pepys MB, Wood SP, The physiological structure of human C-reactive protein and its complex with phosphocholine, Structure, 1999; 7:169-177.
- Pearle AD, Scanzello CR, George S, Mandl LA, DiCarlo EF, Peterson M, et al. Elevated high-sensitivity C-reactive protein levels are associated with local inflammatory findings inpatients with osteoarthritis, Osteoarthritis and Cartilage, 2007; 15:516-523.
- Laureys M, Sion J-P, Slabbynck H, et al. Macromolecular creatine kinase type 1: A serum marker associated with disease, Clin Chem. 1991: 37:430-434.
- Galarraga B, Sinclair D, Fahie-Wilson MN, Mccrae FC, Hull RG, Ledingham JM, A rare but important cause for a raised serum creatine kinase concentration: two case reports and a literature review, Rheumatology, 2003; 42:186-188.
- Rehbein-Thoner M, Pffleiderer, The changes in aldolase isoenzyme pattern during development of the human kidney and small intestine-demonstrated in organ extracts of tissue structure, Physiol Chem, 1977; 358G:169-180.
- Bodian CA, Freedman G, Hossain S, Eisenkraf JB, The visual analog scale for pain: Clinical significance in postoperative patients, Anesthesiology, 2001; 95:1356-1361.

- 22. Bellamy N, Buchnan WW, Goldsmith CH, Campbell J, Stitt LW, Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to anti-rheumatic drug therapy in patients with osteoarthritis of the hip or knee, J Rheumatol, 1988; 15:1833-1840.
- 23. Fairbank JCT, Pynsent PB, The Oswestry Disability Index, Spine, 2000; 25(22):2940-2953.
- 24. Binkley JM, Stratford PW, Lott SA, Riddle DL, The Lower Extremity Functional Scale (LEFS): Scale development, measurement properties, and clinical application, Physical Therapy, 1999; 79:371-383.
- 25. Schag CC, Heinrich RL, Ganz PA, Karnofsky performance status revisited: Reliability, validity, and guidelines, J Clin Oncology, 1984; 2:187-193.
- Ferrera LA, ed. Focus on Body Mass Index and Health Research. New York: Nova Science, 2006. ISBN 978-1-59454-963-2.
- Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD, Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure, J Orthop Sports Phys Ther, 1998; 28(2):88-96.
- 28. Kellgren JH, Lawrence JS, Radiological assessment of osteoarthrosis, Ann Rheum Dis, 1957; 16:494-502.
- American Academy of Orthopaedic Surgeons Joint motion: method of measuring and recording (4thedn). E & S livingstone Publishers, UK: 1965.
- Ganguly A, Tropical phytotherapeutic treatment for achieving knee symmetry in osteoarthritis-a sustainable approach, Int J Phytomed, 2014; 6:489-509.
- 31. Ganguly A, Normalization of varus/valgus deformities in osteoarthritis by external application of phytoconstituents: confirmed with anatomical observations and biochemical profiles and radiological images, Ant Physiol Curr Res, 2016; 6:224.
- 32. Ganguly A, Topical phytotherapy is the nobel approach for revision of total knee replacement: a unique case study, J Orthop Rheumatol, 2018; 5:1-5.
- 33. Lee MJ, Hacquebord J, Varshney A, et al. Risk factors for medical complication after lumbar spine surgery: a multivariate analysis of 767 patients, Spine (Phila Pa 1976), 2011; 36(21):1801-1806.
- 34. Rao SB et al. Risk factors for surgical site infections following spinal fusion procedures: A case-control study, Clin Infect Dis, 2011: 53:686.
- 35. Schoenfeld AJ, Ochoa LM, Bader JO, Belmont PJ, Risk factors for immediate postoperative complications and mortality following spine surgery: A study of 3475 patients from the national surgical quality improvement program, The Journal of Bone & Joint Surgery, 2011; 1577. DOI: 10.2106/JBJS.J.01048
- 36. Reis RC, de Oliveira MF, Rotta JM, Botelho RV, Risk of complications in spine surgery: a prospective study, Open Orthop J, 2015; 9:20-25.
- 37. Passias PG, Poorman GW, Delsole E, Zhou PL, Horn SR, Jalai CM, Vira S, Diebo B, Lafage V, Adverse outcomes and prediction of cardiopulmonary complications in elective spine surgery, Global Spine Journal, 2018; 8(3):218-223.
- 38. Ganguly A, Ganguly D, A novel approach for failed lumbar spine surgery with topical phytotherapeutic treatment: a unique case study, Journal of Drug Delivery & Therapeutics, 2018; 8(6-s):135-140
- 39. Schmorl G, Junganns H, Die gesunde und kranke Wirbelsaule in Rontgenbildund Klinik, Stuttgart, 1951.
- 40. Heliövaara M, Risk factors for low back pain and sciatica, Annals of Medicine, 1989; 21(4):257-264.
- Karahan A, Kav S, Abbasoglu A, Cogan N, Low back pain: Prevalence and associated risk factors among hospital staff, Journal of Advanced Nursing, 2009; 65(3):516-524.
- 42. Begg AC, Falconer MA, Plain radiography in intraspinal protrusion of lumbar intervertebral discs: a correlation with operative findings, Br J Surg, 1949; 36:225-239.
- 43. Hadley LA, Anatomico-roentgenographic studies of the spine, Springfield: Thomas, 1964; 416-417.
- 44. Apple FS, Hellsten Y, Ciarkson PM, Early detection of skeletal muscle injury by assay of creatine kinase MM Isoforms in serum, Clin Chem, 1988; 34(6):1102-1104.
- 45. Belcaro G, Dugall M, Luzzi R, Hosoi M, Ledda A, et al. Phytoproflex®: supplementary management of osteoarthritis: a pilot, open, supplement registry, Minerva Med, 2017; 109:88-94.