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A REVIEW ON INNOVATION IN IMMUNODULATORY THERAPIES FOR NEUROLOGICAL DISORDER FOR ALHEIMER'S DISEASE AND MYASTHENIA GRAVIS

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ABSTRACT

Neuroimmune interactions play a key role in disorders like Alzheimer's disease (AD) and Myasthenia Gravis (MG). Recent immunomodulatory therapies offer targeted approaches to reduce neuroinflammation and slow disease progression. In AD, monoclonal antibodies target beta-amyloid and tau, while microglial modulators, Treg therapies, complement inhibitors, and gut-brain axis interventions support neuroprotection. In MG, therapies include B-cell depletion, complement inhibition, and cytokine targeting. Advanced options like Treg infusions, CAR-T cells, stem cells, and small molecule modulators (e.g., S1P and BTK inhibitors) show promise. Innovations in drug delivery, biomarker-based treatments, and AI-driven drug development are advancing personalized neurology, offering more effective and long-lasting outcomes.

KEYWORDS: Neuroinflammation, Immunotherapy, Autoimmune neurology, Monoclonal antibodies, Cytokine modulation, B-cell targeted therapy, Regulatory T cells.

INTRODUCTION

Neurological disorders such as Myasthenia Gravis (MG) and Alzheimer's disease (AD) are largely caused by neuroimmune interactions. Targeting the underlying immunological malfunction has become more important than managing symptoms due to recent developments in immunomodulatory medicines. These cutting-edge therapeutics, which include gene therapies, cell-based methods, and monoclonal antibodies, seek to balance the immune system and

lessen neuroinflammation. This change represents a significant advancement in neurology, providing more accurate and efficient treatments for neurological conditions linked to the immune system, such as Parkinson's disease (PD), multiple sclerosis (MS), AD, MG, and neuromyelitis optica spectrum disorder (NMOSD) [1-2].

ALZHEIMER'S DISEASE

The main symptoms of Alzheimer's disease (AD), a gradual and fatal neurological illness, are memory loss and cognitive impairment. The buildup of amyloid-β (Aβ) peptides, particularly Aβ42, which creates toxic fibrils, is a significant contributing cause. Aβ42 is structurally composed of disordered residues from positions 1–17 and a β-strand–turn–β-strand motif from positions 18–42. These residues form parallel β-sheets through β1 (residues 18–26) and β2 (residues 31–42). Due to side-chain interactions that encourage unidirectional and cooperative growth, these structures facilitate the creation of fibrils, which in turn causes the deposition of amyloid plaque. An additional characteristic of AD is the development of neurofibrillary tangles, which are brought on by aberrant tau phosphorylation, a microtubule-associated protein that compromises microtubule stability. The development of AD is also aided by oxidative stress, glutamate-induced toxicity, mitochondrial dysfunction, and impaired autophagy. Even though AD has been known for more than a century, its precise origin is still unknown, though therapies that target Aβ are being developed.[3]

Table No.1: Mechanism underlying the neural dysfunction in Alzheimer's disease.

Mechanism	Description	Result
Aβ-amyloid hypothesis	Amyloid plaque resulting from Aβ overproduction or reduced clearance	Aß-amyloid-induced synapto- and neurotoxicity
Aß- amyloid oligomer hypothesis	Soluble oligomers resulting from Aß overproduction or reduced clearance	Aß-oligomer- induced synapto- and neurotoxicity
Ca2+ dysregulation hypothesis	Ca2+ dysregulation due to aging, oxidative stress, Aß, and/or presenilin dysfunction	Ca 2+induced synapto and neurotoxicity
Lysosome hypothesis	Lysosome/ autophagy dysfunction	Impaired proteostasis and axonal transport

MYASTHENIA GRAVIS

Antibodies that block acetylcholine receptors at the neuromuscular junction cause myasthenia gravis (MG), a chronic autoimmune neuromuscular disease marked by weakness and exhaustion. The voluntary muscles, especially those involved in eye movement, facial emotions, chewing, speaking, and swallowing, are weakened by this breakdown in nerve-muscle communication. Double vision (diplopia) and drooping eyelids (ptosis) are typical early symptoms. Most of the time, symptoms get better when you relax and get worse when you exercise. Although MG can affect people of any age, it is more common in women under 40 and in men over 60. Imaging, EMG, antibody testing, and clinical assessment are used in the diagnosis process to find associated disorders such thymomas.[4]

Table No.2: American clinical classification of myasthenia gravis.

Stages	Symptoms
Class I	Any ocular muscle weakness, possible ptosis, no other evidence of muscle weakness elsewhere.
Class II	Mild weakness affecting other than ocular muscles; may also have ocular muscle weakness of any severity.
Class IIA	Predominantly affecting limb, axial muscles, or both; may also have lesser involvement of oropharyngeal muscles.
Class IIB	Predominantly bulbar and/or respiratory muscles; may also have lesser or equal involvement of limb, axial muscles, or both.
Class III	Moderate weakness affecting other than ocular muscles; may also have ocular muscle weakness

	of any severity.
Class IIIA	Predominantly affecting limb, axial muscles, or both; may also have lesser involvement of oropharyngeal muscles.
Class IIIB	Predominantly bulbar and/or respiratory muscles; may also have lesser or equal involvement of limb, axial muscles, or both.
Class IV	Severe weakness affecting other than ocular muscles; may also have ocular muscle weakness of any severity.
Class IVA	Predominantly affecting limb, axial muscles, or both; may also have lesser involvement of oropharyngeal muscles.
Class IVB	Predominantly bulbar and/or respiratory muscles; may also have lesser or equal involvement of limb, axial muscles, or both (Can also include feeding tube without intubation).
Class V	Intubation needed to maintain airway, with or without mechanical ventilation.

Clinical assessment, antibody testing, EMG, and imaging are used to diagnose myasthenia gravis (MG) and to rule out similar disorders including thymomas. Although there isn't a cure, drugs like immunosuppressants, corticosteroids, anticholinesterase medicines, and monoclonal antibodies can help control it.[5] In certain situations, a thymectomy might be advised. Most people can have regular or nearly normal lives if they receive the right care. Controlling symptoms and enhancing quality of life need early diagnosis and a thorough treatment strategy, and current research gives hope for future developments.[3]

IMMUNODULATORY THERAPIES

Immunomodulatory therapies control or modify the activity of the immune system by either boosting weaker immunological responses or decreasing hyperactive ones.[6,7] These treatments are essential for the treatment of cancer, allergies, autoimmune illnesses, and organ transplantation. Immunomodulators, such as monoclonal antibodies (like rituximab) and TNF-alpha inhibitors (like infliximab), target particular immune components to reduce inflammation and prevent tissue damage in autoimmune diseases like MS, rheumatoid arthritis, and MG. Immune checkpoint medications such as pembrolizumab and nivolumab improve T-cell responses to target malignancies in cancer.[8] In neurological conditions including MS, NMOSD, AD, and MG, where immunological dysfunction results in inflammation and nerve damage, immunomodulatory therapy is also essential.[9]

Immunomodulators are classified into several categories which is shown in Table No.3 [7].

Table No. 3: Classification for Immunodulatory Therapies.

Types	Function
Corticosteroids	Broad-spectrum immunosuppressants used in many inflammatory conditions.
Biologic agents	Targeted therapies like monoclonal antibodies that act on specific immune molecules or cells.
Cytokine therapies	Use of signalling proteins like interferons to modulate immune responses.
Small molecule inhibitors	Drugs such as JAK inhibitors, which block intracellular pathways involved in immune cell activation.

IMMUNODULATORY THERAPIES FOR ALZHEIMER DISEASE

Amyloid-beta (Aβ) plaques, tau tangles, and persistent neuroinflammation are the main causes of Alzheimer's disease (AD), a progressive neurodegenerative illness characterized by memory loss, cognitive decline, and behavioral abnormalities. While current developments highlight immunomodulatory medications that address the underlying illness pathways, traditional treatments concentrate on symptom management.[8,9] In AD, overactivated microglia contribute to neuronal damage by releasing pro-inflammatory cytokines such as IL-1β, TNF-α, and IL-6. Shifting microglial activity toward a neuroprotective role is the goal of immunotherapies. Although side effects like ARIA are

still a worry, monoclonal antibodies like aducanumab, lecanemab, and donanemab target Aβ plaques, lowering their buildup and modifying immune responses. To stop tau aggregation and the inflammation it causes, tau-targeted treatments like semorinemab are also being developed. These new methods show promise in moving away from symptomatic treatment and toward disease-modifying tactics that target AD's protein pathology and immunological dysregulation.[10,11]

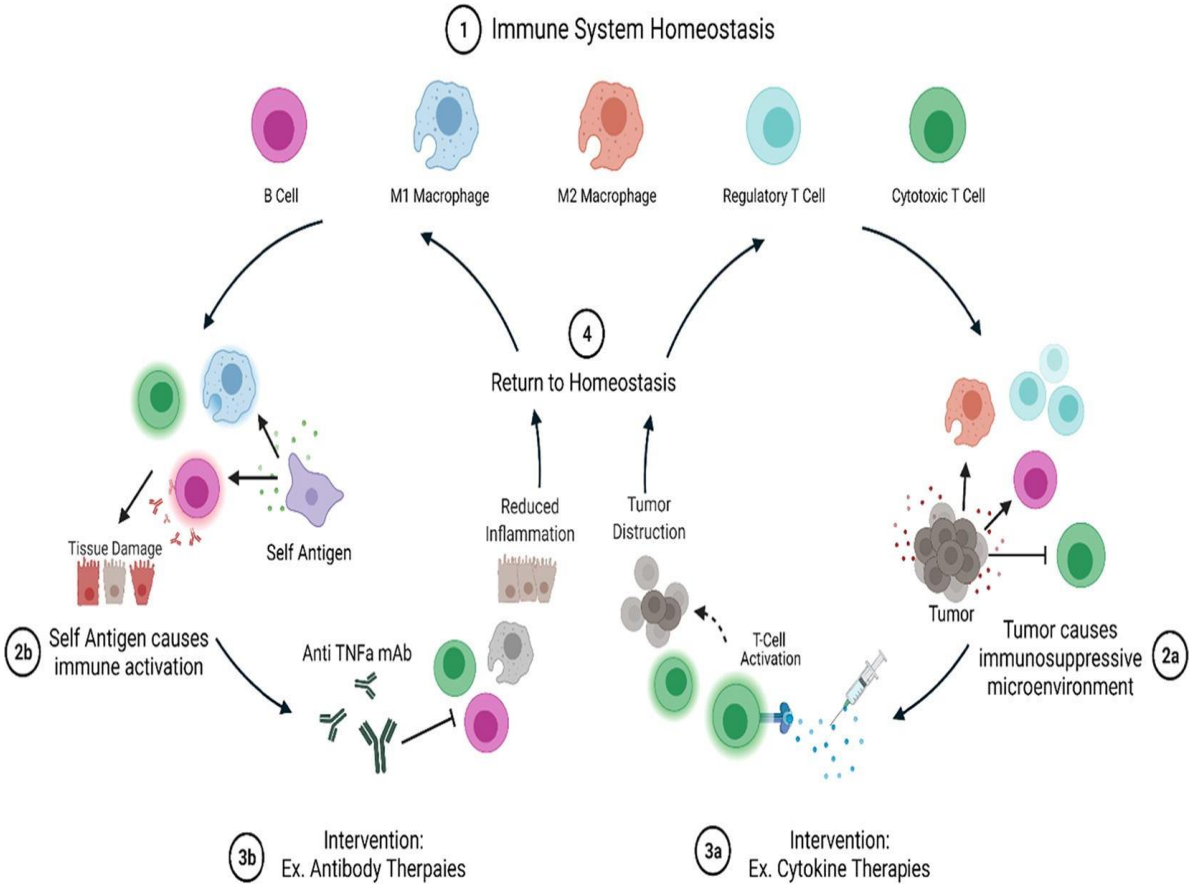

Figure No.1: Immune system in homeostasis.

TYPES OF THERAPIES FOR ALHEIMER'S DISEASE

MONOCLONAL ANTIBODIES (mAbs): Monoclonal antibodies (mAbs) are now vital components of immunomodulatory treatments, providing focused methods for the treatment of inflammatory and autoimmune disorders. Unlike conventional immunosuppressants, these antibodies modify immune responses by selectively binding to cytokines, cell receptors, or immunological checkpoints, improving treatment outcomes and reducing adverse effects.[12]

Adalimumab, a completely human monoclonal antibody that targets the cytokine tumor necrosis factor-alpha (TNF-α), which contributes to chronic inflammation, is one well-known example. By inhibiting inflammatory pathways, it is frequently used to treat psoriasis, Crohn's disease, and rheumatoid arthritis.[14-15] Tocilizumab, another important antibody, has demonstrated effectiveness in treating cytokine release syndrome and rheumatoid arthritis by blocking the interleukin-6 (IL-6) receptor.[13]

Monoclonal Antibodies Also Includes

- **Targeting Aβ and Tau.** Monoclonal antibodies (mAbs) targeting amyloid-beta (Aβ) and tau proteins have become central to immunomodulatory strategies for treating neurodegenerative diseases, particularly Alzheimer's disease (AD). These pathological proteins are hallmarks of AD, with Aβ forming extracellular plaques and tau aggregating into neurofibrillary tangles. By directing the immune system to clear these toxic accumulations, mAbs offer a targeted and promising therapeutic approach.[16]

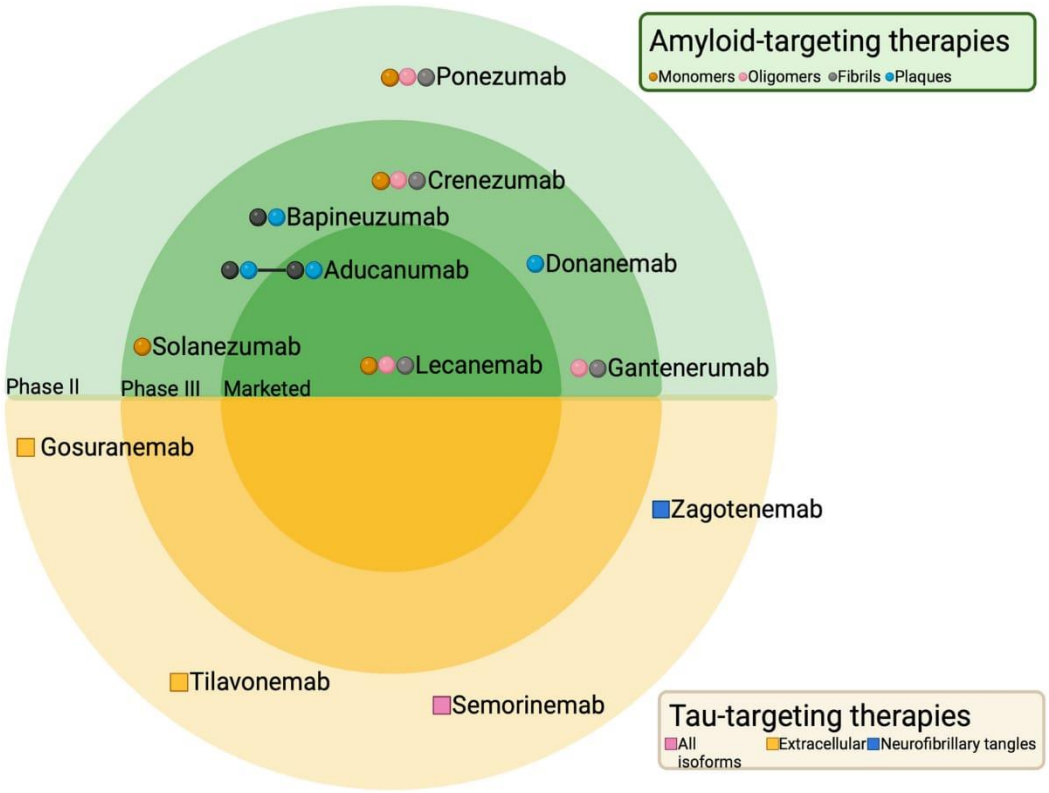

Figure No. 2: Immunotherapy targeting amyloid and tau protein.

MICROGLIA MODULATION

The development of Alzheimer's disease (AD) is significantly influenced by microglia, which are the immune cells that dwell in the brain. Recent studies have demonstrated the potential of immunomodulatory treatments that target microglial activation to lessen neuroinflammation and amyloid-beta buildup, two important pathogenic characteristics of AD.[17,18]

Microglia modulation also includes:

TREM 2 Agonist: In the context of Alzheimer's disease (AD), Triggering Receptor Expressed on Myeloid Cells 2 (TREM2) is a crucial regulator of microglial function. TREM2 activation increases phagocytosis of amyloid-beta plaques and supports neuroprotection by promoting microglial survival, proliferation, and transformation into a disease-associated phenotype.[19,20].

- **Colony Stimulation Factors 1 Receptor (Csf1r) Inhibitor**

Microglia are the immune cells that live in the brain, and their survival and growth depend on the Colony Stimulating Factor 1 Receptor (CSF1R). Chronic activation of microglia in Alzheimer's disease (AD) leads to persistent

neuroinflammation and neuronal destruction. CSF1R inhibitors, which target microglial overactivation, have become attractive options in immunomodulatory therapy.[21,22]

REGULATORY T_{CELL} (T_{REG}) THERAPIES: Regulatory T cells (Tregs) play a crucial role in maintaining immune homeostasis and suppressing chronic inflammation. In Alzheimer'sdisease (AD), impaired Treg function has been linked to increased neuroinflammation and accelerated disease progression. Treg-based therapies aim to restore immune balance byenhancing Treg activity, which can indirectly modulate microglial behavior toward a moreanti-inflammatory, neuroprotective state. Preclinical studies show that boosting Tregpopulations can reduce microglial activation, lower amyloid-beta burden, and improvecognitive outcomes. These findings highlight Treg therapy as a promisingimmunomodulatory strategy for altering microglial responses in AD.[23-25]

Regulatory T_{cell} (T_{reg}) Therapies also includes:

- **IL-2 Therapy:** Interleukin-2 (IL-2) therapy has emerged as a promising strategy to enhance regulatory T cell (Treg) function in Alzheimer's disease (AD). Low-dose IL-2 selectively expands Tregs without activating pro-inflammatory immune cells, thus promoting an anti-inflammatory environment. Enhanced Treg activity helps suppress overactive microglia, reducing neuroinflammation and supporting neuronal survival.[25].
- **T_{reg} infusion:** Interleukin-2 (IL-2) therapy has emerged as a promising strategy to enhance regulatory T cell (Treg) function in Alzheimer's disease (AD). Low-dose IL-2 selectively expands Tregs without activating pro-inflammatory immune cells, thus promoting an anti-inflammatory environment. Enhanced Treg activity helps suppress overactive microglia, reducing neuroinflammation and supporting neuronal survival[26].

COMPLEMENT SYSTEM INHIBITOR: Complement system inhibitors represent a promising addition to regulatory T cell (Treg)-based therapies in immunomodulatory approaches for Alzheimer's disease (AD). Overactivation of the complement system contributes to chronic neuroinflammation and microglial overactivation, exacerbating neuronal damage.[27]

Complement system inhibitors includes:

- **ANX005 & CIq Inhibitors:** ANX005 and C1q inhibitors are emerging complement system-targeted therapies that may enhance regulatory T cell (Treg) efficacy in Alzheimer's disease (AD). ANX005, a monoclonal antibody against C1q, blocks the initiation of the classical complement pathway, thereby reducing synaptic loss and neuroinflammation. These therapies offer a promising combined approach for modulating innate immunity and enhancing neuroprotection in AD.[28]

IMMUNODULATORY THERAPIES FOR MYASTHENIA GRAVIS: Immunomodulatory therapy plays a critical role in managing Myasthenia Gravis (MG), an autoimmune neuromuscular disorder characterized by fluctuating muscle weakness. Treatments such as corticosteroids, intravenous immunoglobulin (IVIG), plasma exchange (PLEX), and newer monoclonal antibodies like eculizumab help suppress abnormal immune responses and reduce autoantibody activity. Advances in biologics and targeted therapies continue to expand treatment options for MG.[29]

COMPLEMENT INHIBITOR: Complement inhibitors represent a targeted immunomodulatory approach in treating Myasthenia Gravis (MG), particularly in patients with anti-acetylcholine receptor antibodies.[30]

- **Ecolizumub and Ravulizumab (FDA approval C5 inhibitor): :** Eculizumab and ravulizumab are FDA-approved complement C5 inhibitors used in the immunomodulatory treatment of generalized Myasthenia Gravis (gMG) in patients positive for anti-acetylcholine receptor antibodies. These monoclonal antibodies block the terminal complement cascade, preventing destruction at the neuromuscular junction. Eculizumab, the first approved, demonstrated significant symptom improvement in refractory gMG.[30]
- **Zilucoplan:** Zilucoplan is a subcutaneously administered, FDA-approved complement C5 inhibitor used in the treatment of generalized Myasthenia Gravis (gMG) in adults with anti-acetylcholine receptor antibodies. It blocks the cleavage of complement component C5, preventing the formation of the membrane attack complex, which contributes to neuromuscular junction damage. Clinical trials have shown that zilucoplan significantly improves muscle strength and daily functioning while offering the convenience of self-administration. As a targeted immunomodulatory therapy, it provides an effective and less invasive alternative to intravenous complement inhibitors, advancing the management of refractory gMG.[31]

B cell DEPLETION THERAPY: B cell depletion therapy has emerged as a promising immunomodulatory approach in Myasthenia Gravis (MG), targeting the source of pathogenic autoantibodies. Rituximab, a monoclonal antibody against CD20 on B cells, has shown particular efficacy in MuSK antibody-positive MG, reducing relapse rates and improving muscle strength.[32]

- **Rituximab (anti - CD20 mAb:** Rituximab, an anti-CD20 monoclonal antibody, is a key agent in B cell depletion therapy for Myasthenia Gravis (MG), particularly effective in MuSK antibody-positive patients. By targeting CD20 on B cells, rituximab reduces the production of autoantibodies that disrupt neuromuscular transmission[33].
- **Inebilizumab:** Inebilizumab is a humanized monoclonal antibody that targets CD19, offering a broader range of B cell depletion compared to CD20-directed therapies. Early data suggest that inebilizumab may provide durable symptom relief with manageable safety. Ongoing clinical trials are evaluating its efficacy and long-term safety in MG treatment.[34]

Tcell MODULATION: While inebilizumab primarily targets CD19-positive B cells, its immunomodulatory effects may also indirectly influence T cell activity in Myasthenia Gravis (MG). By depleting B cells and plasmablasts that present antigens and support autoreactive T cells, inebilizumab may reduce pathogenic T cell responses involved in MG progression.[35]

- **Abatacept (CTLA-4Ig):** Abatacept (CTLA-4Ig) is a fusion protein that modulates T cell activation by blocking the CD28-CD80/86 co-stimulatory pathway, thus inhibiting T cell proliferation and cytokine release.[30]
- **IL-6 inhibitors:** Interleukin-6 (IL-6) inhibitors, such as tocilizumab, modulate T cell activity and have shown promise in treating refractory Myasthenia Gravis (MG). IL-6 is a pro-inflammatory cytokine that promotes differentiation of pathogenic Th17 cells and supports B cell activation, both critical in MG pathogenesis.[36]

CAR-T and TREG-BASED THERAPIES: Emerging immunomodulatory therapies for Myasthenia Gravis (MG) include chimeric antigen receptor T cell (CAR-T) and regulatory T cell (Treg)-based approaches. CAR-T therapies are engineered to target autoreactive B cells, offering highly specific immune modulation. Meanwhile, Treg-based therapies aim to restore immune tolerance by enhancing or expanding regulatory T cells that suppress pathogenic T and B cell responses.[37]

- **T cells (Car-Tregs) In Car-T And Treg-Based Therapies:** Engineered regulatory T cells (CAR-Tregs) represent a cutting-edge immunomodulatory strategy for treating Myasthenia Gravis (MG).[38]
- **Treg-enhancing therapies:** Treg-enhancing therapies aim to restore immune tolerance in Myasthenia Gravis (MG) by boosting the number or function of regulatory T cells (Tregs), which suppress autoreactive immune responses. Strategies include low-dose interleukin-2 (IL-2) therapy, which selectively expands Tregs, and small molecules or biologics that promote Treg stability and activity.[54]

Table No 4: Comparative Overview of Emerging Therapies for Alzheimer's Disease and Myasthenia Gravis.

Therapy Type	Alzheimer's Disease (AD)	Myasthenia Gravis (MG)
Monoclonal Antibodies	- **Leqembi (lecanemab)**: Targets amyloid beta to reduce plaque buildup; approved in the EU for early AD.	- **Vyvgart (efgartigimod alfa)**: FcRn inhibitor that reduces pathogenic IgG antibodies; approved in the US and EU.
	- **Trontinemab (RG6102)**: Utilizes Brainshuttle™ technology to enhance brain penetration; in clinical trials.	- **Zilucoplan**: Complement C5 inhibitor; approved in the US and EU.
Cell-Based Therapies	- **Mesenchymal Stromal Cells (MSCs)**: Show promise in reducing inflammation and promoting neurogenesis; under investigation.	- **CAR-T Cell Therapies**: Descartes-08 (mRNA-based) and MuSK-CAAR-T (MuSK-specific); early-stage trials show durable responses.
Gene Therapies	- **Tau-Lowering Agents**: Investigational drugs targeting tau protein to prevent neurofibrillary tangles; in development.	- **Not yet established**
Other Emerging Strategies	- **Anti-Inflammatory Agents**: Drugs like liraglutide and semaglutide being explored for their potential benefits in AD.	- **Plasmapheresis and Immunoadsorption**: Used in acute exacerbations to remove pathogenic antibodies.

DISCUSSION

The advancement of immunomodulatory therapies has redefined the therapeutic landscape for neurological disorders with autoimmune and inflammatory etiologies, particularly Alzheimer's Disease (AD) and Myasthenia Gravis (MG). The traditional approach of managing symptoms with broad-spectrum immunosuppressants is now being supplemented—and in some cases replaced—by targeted biological and cellular therapies that aim to address the underlying pathophysiology.

In AD, monoclonal antibodies targeting amyloid-beta (Aβ) and tau proteins have shown promise in reducing pathological aggregations that contribute to neurodegeneration. The approval of agents like aducanumab and lecanemab highlights a shift toward disease-modifying treatments, although debates persist regarding their clinical effectiveness and risk-benefit profile, especially with side effects such as amyloid-related imaging abnormalities (ARIA). Furthermore, strategies targeting microglial modulation using TREM2 agonists and CSF1R inhibitors, as well as regulatory T cell (Treg) therapies, signify an emerging focus on controlling neuroinflammation. Notably, the integration of gut-brain axis interventions, such as probiotics and fecal microbiota transplantation, introduces a novel and relatively unexplored frontier in neuroimmune therapy.

On the other hand, MG represents a more well-characterized autoimmune disorder, where immunomodulation has yielded robust clinical success. Treatments such as complement C5 inhibitors (eculizumab, zilucoplan) and B cell depletion therapy (rituximab) have transformed the management of generalized MG, especially in treatment-resistant cases. Recent cellular therapies, including CAR-Tregs and mesenchymal stem cell therapy, provide long-term modulation of autoreactive immune responses, offering durable remission and reduced dependence on corticosteroids.

Despite these innovations, several challenges remain. In AD, the complexity of disease mechanisms, blood-brain barrier penetration issues, and variability in patient responses limit the widespread success of immunotherapies. In MG, although newer therapies are effective, accessibility and cost continue to be significant barriers, and long-term safety data are still emerging.

Overall, the growing understanding of immune mechanisms in neurological disorders is driving the development of precision immunotherapies, tailored to the immunological profile and disease stage of individual patients. These therapies are not only advancing clinical care but also stimulating further research into biomarkers, drug delivery systems, and personalized neurology.

CONCLUSION

Immunomodulatory therapies represent a transformative approach in the management of neurological disorders such as Alzheimer's Disease and Myasthenia Gravis. While both conditions share a basis in immune dysfunction, their therapeutic landscapes differ in maturity and efficacy. In MG, targeted therapies such as complement inhibitors and B cell depleting agents have demonstrated clear clinical benefits and have redefined treatment standards. In contrast, AD remains a more complex challenge; although monoclonal antibodies and microglial modulators show promise, their efficacy varies, and associated risks warrant caution.The review highlights several emerging modalities—including Treg therapies, gene therapy, cell-based interventions, and AI-driven drug discovery—that are reshaping the future of neurological care. These innovations signify a shift from symptomatic treatment to mechanism-based, disease-modifying strategies that aim to restore immune balance, reduce neuroinflammation, and prevent neurodegeneration.

However, the road ahead demands rigorous clinical validation, long-term safety monitoring, cost-effectiveness assessments, and accessibility considerations. Tailoring these therapies to individual patients using biomarkers and real-time monitoring tools will be critical to achieving optimal outcomes. Interdisciplinary collaboration among neurologists, immunologists, pharmacologists, and bioengineers will further accelerate this paradigm shift.

In conclusion, immunomodulatory therapy holds great potential to revolutionize the treatment of neurological disorders, offering personalized, targeted, and more durable outcomes. Continued research, patient-centric clinical trials, and real-world evidence will be key to unlocking its full potential and translating scientific innovation into standard clinical practice.

REFERENCES

1. Krati, Dr. Martolia Jaya, et. al, A comprehensive review on in-vitro methods for anti- microbial activity, IP International Journal of Comprehensive and Advanced Pharmacology, 2024; 9(3).
2. Neeru, Shilpi Kashyap, Esha Vatsa, Jitendra Singh and Ankush Sundriyal "Determination of Total Phenolic Content, Total flavonoid Content and Total Antioxidant capacity of different extracts of Roylea elegans Wall. (aerial parts)" World journal of pharmacy and pharmaceutical sciences (WJPPS), 2016; 5(6): 1884-1891.
3. Neeru, Esha Vatsa, Jitendra Singh and Ankush Sundriyal "Pharmacognostic Standardization Parameters of Roylea elegans Wall. (Aerial Parts)" International Journal for Pharmaceutical Research Scholars (IJPRS), 2016; 5(2): 133-140.
4. Kundan Singh Bora and Esha Vatsa "Pharmacognostic Evaluation of Dendrobium macraei Lindl." Universities Journal of Phytochemistry and Ayurvedic Heights (UJPAH), 2016; 1(20): 29-36.

5. Amit Sharma, Bharat Parashar, Esha Vatsa, Shilpa Chandel and Surbhi Sharma "Phyto chemical screening and Anthelmintic activity of leaves of Cedrus deodara (Roxb.)" World journal of pharmacy and pharmaceutical sciences (WJPPS), 2016; 5(8): 1618-1628.
6. Amit Sharma, Surbhi Sharma, Shilpa Chandel, Esha Vatsa and Dr. Bharat Parashar "A review on Morchella esculanta: Therapeutically Potent plant" World journal of pharmacy and pharmaceutical sciences (WJPPS), 2016; 5(9): 685- 699.
7. Esha Vatsa and Kundan Singh Bora "Memory Enhancing Activity of Dendrobium macraei Lindl. in Swiss Albino Mice" British Journal of Pharmaceutical Research (BJPR), 2016; 13(2): 1-11.
8. Vatsa Esha, Chandel Shilpa, Parashar Bharat, Neeru "Physico-Chemical and Phytochemical Evaluation of Dendrobium macraei Lindl. (Whole Plant)" International Journal of Pharmacognosy and Phytochemical Research (IJPPR), 2016; 8(11): 1801-1811.
9. Esha Vatsa, Mehak Aggarwal, Shipra Gautam "Formulation and Evaluation of Polyherbal Facial Scrub" Just Agriculture multidisciplinary e-Newsletter, Article ID: 023, 2021; 1(9): 1-6.
10. Shipra Gautam, Madhubala Thakur, Mehak Aggarwal, Esha Vatsa "Azadirachta indica- A Review as a Potent Anti- Diabetic drug" Just Agriculture multidisciplinary e-Newsletter, Article ID:98, 2021; 1(10): 1-6.
11. Esha Vatsa, Samriti Faujdar, Nidhi Sharma, Shilpa Chandel, Mehak Aggarwal "Dendrobium macraei Lindl.: A review on medicinally potent orchid on the basis of recent evidences" Chinese Journal of Medical Genetics, 2022; 31(3): 560-571.
12. Krati, Babita Rawat, Abhishek Bhardwaj, Amandeep Singh, A Comprehensive Review on Indian Barnyard Millet (Echinochloa frumentacea), International Journal of Pharmaceutical Technology and Biotechnology, 2025; 12(1): 01-07.
13. Krati, Dr. Martolia Jaya, et. al, A Comprehensive review on in-vitro methods for antimicrobial activity" Educational administration: Theory and Practice". 2024; 30(6): 8 (2977-2984).
14. Esha Vatsa, Dr. Samriti Faujdar, Shilpa Chandel, Nidhi Chaudhary, Ashok Kumar, Neeru, "Studies on anti-inflammatory activities of whole plant of Dendrobium macraei Lindl." European Chemical Bulletin, 2023; 12(Special Issue 1): 657-664.
15. Esha Vatsa, Dr. Samriti Faujdar, Nitin Kumar, Nidhi Chaudhary, Shilpa Chandel, Neeru, Mehak Aggarwal "Current studies to justify the medicinal potential of the orchid Dendrobium macraei Lindl." European Chemical Bulletin, 2023; 12(S3): 5822-5830.
16. Divya Negi Rawat, Anjali Bisht, Esha Vatsa, Deepika Chandra, Nidhi Chaudhary, Ashok Kumar "Urinary bacterial profile and antibiotic susceptibility pattern among patients of urinary tract infections" High Technology letters, 2023; 29(10): 115-128.
17. Mehak Aggarwal, Ujjwal Nautiyal, Harmeet Singh, Esha Vatsa, Nidhi Chaudhary, Anjali Bisht, Divya Negi "Development and evaluation of drug delivery system containing luliconazole" High Technology letters, 2023; 29(11): 633-652.
18. Jagriti Gairola, Prashant Kukreti, Anjali Bisht, Divya Negi, Nidhi Chaudhary, Esha Vatsa "Development of Chronotherapeutic Delivery System for the Oral Administration of Aceclofenac for Rheumatoid Arthritis by Using Different Polymers" Journal of Chemical Health Risks, 2023; 13(6): 1180-1192.

19. Nidhi Chaudhary, Dr. Deepak Nanda, Dr. Esha Vatsa, Mithilesh Kesari, Harshita Chandra, Simran Singh Rathore "The Promise of Usefulness of the Evergreen Shrub Cassia auriculata" Journal of Advanced Zoology, 2023; 44(4): 1249-1261.
20. Ms Pooja Yadav, Dr. Esha Vatsa, Dr Arti Rauthan, "Enhancing Menstrual Awareness among Adolescent Girls: Evaluating the Influence of School Initiatives" Journal of Chemical Health Risks, 2024; 14(02): 3141-3149.
21. Mehak Aggarwal, Esha Vatsa, Nidhi Chaudhary, Shilpa Chandel, Shipra Gautam, "Formulation and Evaluation of Polyherbal Face Pack" Research Journal of Pharmacy and Technology, 2024; 17(6): 2481-2485.
22. Esha Vatsa, Mehak Aggarwal, Nidhi Chaudhary, Shipra Gautam, Neeru, Nitin Kumar, "Comparison Based on Pharmacognostical and Pharmacological Profile of Thuja Orientalis Linn. And Thuja Occidentalis Linn.: A Review" Naturalista Campano, 2024; 28(1): 3208-3219.
23. Priya Pandey, Esha Vatsa, Gaurav Lakhchora, Md Shamsher Alam, Niyaz Ahamad Ansari, Mohammad Dabeer Ahamad, Sarafarz Ahamad, Mukul Singh, Nitin kumar, "Nano Medicine Advancements in Addressing Rare Neurological Disorders: A Focus on Globoid Cell Leukodystrophy (Krabbe's Disease) Treatment" African Journal of Biological Sciences, 2024; 6(3): 2654-2684.
24. Esha Vatsa, Nidhi Chaudhary, Priya Khadwal, Mehak Aggarwal, Tanya Aggarwal, and Nishant Bhardwaj, "In vitro Antidiabetic Effect and Phytochemical Screening of Cassia biflora Mill." Indian Journal of Natural Sciences, 2025; 15(88): 87726-87733.
25. Anil Kumar, Dr. Esha Vatsa, "AI-Powered Embryo Selection is revolutionized: A Review" South Eastern European Journal of Public Health, 2025; XXVI (1): 6223-6230.
26. Lohani, V., A R, A., Kundu, S., Akhter, M. Q., & Bag, S. Single-Cell Proteomics with Spatial Attributes: Tools and Techniques. ACS omega, 2023; 8(20): 17499–17510. https://doi.org/10.1021/acsomega.3c00795.
27. Amandeep Singh, Deepak Nanda, Ashok Kumar and Abhishek Bhardwaj. In vitro evaluation of anti-inflammatory activity of ageratum conyzoides leaves by Human Red Blood Cell (HRBC) membrane stabilization method, International Journal of Research in Pharmaceutical and Nano Sciences, 2023; 12(6): 196-202.
28. Amandeep Singh, Deepak Nanda, Ashok Kumar, Abhishek Bhardwaj. In vitro evaluation of anti-inflammatory activity of ageratum conyzoides leaves by Human Red Blood Cell (HRBC) membrane stabilization method, International Journal of Research in Pharmaceutical and Nano Sciences, 2023; 12(6): 196-202.
29. Singh A, Nanda D, Bhardwaj A, Kumar A. A pharmacological investigation for therapeutic potential of Callistemon citrinus as an anthelmintic agent (Bottle-Brush Plant). IP Int J Comprehensive Adv Pharmacol, 2024; 9(3): 206-210.
30. Yogesh Tiwari, Amandeep Singh, Bhupendra Kumar, Ashok Kumar. "In Vitro Evaluation of Alpha Amylase Activity of Bark Extracts of Ficus Auriculata". International Journal of Innovative Science and Research Technology. December, 2017; 2(12): 88-92.
31. Bhupendra Kumar, Amandeep Singh, Yogesh Tiwari, Ashok Kumar. UV PROTECTIVE ACTIVITY OF GLYCINE MAX SEEDS. Indian Research Journal of Pharmacy and Science, 2017; 15: 1190-1195.
32. Reena Bhatt, Ashok Kumar, Ankita Sharma. Formulation and evaluation of shampoo formulated by glycine max seeds. Indian Research Journal of Pharmacy and Science; 15(2017): 1232-1238.
33. Kumar A, Nanda D and Gupta A. "A Prospective Study on the Risk Determinants and Economic Burden of Adverse Drug Reactions in Tertiary Care Hospital". Indian Journal of Natural Sciences, 2025; 15(88): 87957-87961.

34. Ashok Kumar, Deepak Nanda and Abhishek Gupta A holistic approach to adverse drug reactions in hospitals: Classification, risk factors, assessment and economic evaluation- A review. J. Exp. Zool. India, 2024; 27: 2337-2348. DOI: https://doi.org/10.51470/jez.2024.27.2.2337
35. Sakshi Garg, Ashok Kumar, Varsha Deva, Preeti Biswas, Harsh Rastogi, Heena Farooqui. Immediate-Release Drug Delivery System, Current Scenario, and Future Perspective-A Narrative Review. Jundishapur Journal of Microbiology, 2022; 15(1): 6509-6519.
36. Ashok Kumar, Deepak Nanda, Abhishek Gupta Pattern of Adverse Drug Reactions and Their Economic Impact on Admitted Patients in Medicine Wards of a Tertiary Care Hospital. Library Progress International, 2024; 44(4): 1120-1139.
37. Alisha Rawat, Meenakshi Sajwan, Yamini Chandola, Nidhi Gaur "Assaultive role of thiamine in coalition with selenium in treatment of liver cancer", Journal of emerging technologies and innovative research, 2022; 9(1); 2349-5162.
38. Ghildiyal, P., Bhatt, A., Chaudhary, N., Narwal, S.,Sehgal, P. "Study of various biochemical parameters on atrazine induced glucose-6-phosphate dehydrogenase deficiency in brain" International Journal of Health Sciences, 2022; 6(S7): 2552-2558.
39. Alok Bhatt, Arun Kumar, Pallavi Ghildiyal, Jyoti Maithani, Nidhi Chaudhary, Manish Nawani, Sonia Narwal "Phytochemical Profile of Melissa parviflora Benth" Neuro Quantology, 2022; 20(9); 2426-2428.
40. Palika Sehgal, Alok Bhatt, Sonia Narwal, Deepak P. Bhagwat, Nidhi Chaudhary et.al Formulation Characterization Optimization and In Vitro Evaluation of Aceclofenac Topical Emulgel, Neuro Quantology, 2022; 20(14): 1-09.
41. Sneha Rawat, Praveen Kumar Ashok, Abhishek bhardwaj "A review on Oro dispersible Tablet of Telmisartan" Org-Journal of Emerging Technologies and Innovative research (JETIR), May 2023; 10(5):i104-i112.
42. Jaison Varghese, Nitin kumar, Sapna Chaudhar, Abhishek Bhardwaj(2024) "Comparative In-Vitro Antioxidant and Antimicrobial Potential of Some Medicinal Plants" African Journal of Biological Sciences, https://doi.org/10.48047/AFJBS.6.Si3.2024.3340-3346.
43. Asima Imtiyaz, Ajay Singh, Abhishek Bhardwaj(2024) "Green synthesis of iron oxide nanoparticles from Iris kashmiriana (Mazar-Graveyard) Plant Extract its characterization of biological activities and photocatalytic activity" Journal of Industrial and Engineering Chemistry, https://doi.org/10.1016/j.jiec.2024.09.004.
44. Hem Chandra Pant, Bhawana Goswami, Ashok Kumar, Abhishek Bhardwaj, Shanti Rauthan and Amita pandey "A Review Paper on Bacopa monniera and Role of Artificial Intelligence (AI) in Medicinal Plant for Management and Treatment of Various Diseases" Indian Journal of Natural Sciences, 2025; 15(88): 01-10.
45. Vishwajeet Bachhar, Vibha Joshi, Ajay Singh, M. Amin Mir, Abhishek Bhardwaj(2025)"Antibacterial, Antioxidant, and Antidiabetic Activities of TiO2 Nanoparticles Synthesized Through Ultrasonication Assisted Cold Maceration from Stem Extract of Euphorbia hirta" Nano Bioscience, https://doi.org/10.33263/LIANBS141.001.
46. Nidhi Chaudhary, "A review on: The deciduous shrub "Punica granatum", European journal of biomedical and pharmaceutical sciences, 2016; 3(7); 2349-2388.
47. Singh Harmeet and Nidhi Chaudhary, "Evaluation of Lakshadi Guggul on experimentally induced global cerebral ischemia/reperfusion injury". World journal of Pharmacy and Pharmaceutical Sciences, 2016; 6(1); ISSN 2278-4357.

48. Nidhi Chaudhary and Harmeet Singh, "Evaluation of Punica Granatum Leaves Extract In Scopolamine Induced Learning And Memory Impairment In Mice". World journal of Pharmacy and Pharmaceutical Sciences, 6(6); 1677-1703.
49. Amandeep Singh, Pankaj Nainwal, Deepak Nanda,D.A. Jain, SOLUBILITY ENHENCEMENT OF PIOGLITAZONE WITH COMPLEXATION OF HYDROXYPROPYL-β-CYCLODEXTRIN, Digest Journal of Nanomaterials and Biostructures, Apr 2012 2(4): p.91-97.
50. Pankaj Nainwal Deepak Nanda, Amandeep Singh, D. A. Jain, Quantitative spectrophotometric determination of domperidone tablet formulations using ibuprofen sodium as hydrotropic solubilizing agent, Digest Journal of Nanomaterials and Biostructures, 2012; 2(4): 751 – 753
51. Deepak Nanda, Pankaj Nainwal, Amandeep Singh, D.A.Jain, Review on mixed-solvency concept: a novel concept of solubilization, Deepak Nanda et al.,Journal of Pharmacy Research, 2012; 3(2):411-413
52. Pankaj Nainwal, Amandeep Singh, Deepak Nanda, D.A.Jain, NEW QUANTITATIVE ESTIMATION OF ROSUVASTATIN BULK SAMPLE USING SODIUM BENZOATE AS HYDROTROPIC SOLUBILIZING AGENT, Journal of Pharmacy Research, 2012; 3(1): 6-8
53. Nainwal.P, Bhagla.A, Nanda.D, STUDY ON ANTIOXIDANT POTENTIAL AND WOUND HEALING ACTIVITY ON THE AQUEOUS EXTRACT OF FRUITS OF GARCINIA MANGOSTANA, IJPI's Journal of Pharmacognosy and Herbal Formulations, Volume-1
54. Pankaj Nainwal, Kapil Kalra, Deepak Nanda, Amandeep Singh, STUDY OF ANALGESIC AND ANTI-INFLAMMATORY ACTIVITIES OF THE ETHANOLIC EXTRACT ARIAL PARTS OF FUMARIA VAILLANTII LOISEL, Asian Journal of Pharmaceutical and Clinical Research, 2011; 4(1).
55. Amandeep Singh, Pankaj Nainwal, Deepak Nanda, D.A.Jain, SOLUBILITY ENHANCEMENT STUDY OF PIOGLITAZONE USING SOLID DISPERSION AS SOLUBILIZATION TECHNIQUE, International Journal of Science Innovations and Discoveries, Amandeep Singh et al., IJSID, 2011; 1(2): 95—100
56. Amandeep Singh, Pankaj Nainwal, Deepak Nanda, D. A. Jain, THE SOLUBILITY ENHANCEMENT STUDY OF PIOGLITAZONE USING DIFFERENT SOLUBLIZATION TECHNIQUIES, International Journal of Pharmacy & Pharmaceutical Sciences, 2012; 4(2).
57. Deepak Nanda, Pankaj Nainwal, Amandeep Singh, D.A.Jain, SOLUBILITY ENHANCEMENT STUDY OF DOMPERIDONE USING DIFFERENT SOLUBILIZATION TECHNIQUES, International Journal of Pharmacy and Pharmaceutical Sciences 2012; 2(3).
58. Pankaj Nainwal, Priyanka Sinha, Amandeep Singh, Deepak Nanda, D.A.Jain, A COMPARATIVE SOLUBILITY ENHANCEMENT STUDY OF ROSUVASTATIN USING SOLUBILIZATION TECHNIQUES, International Journal of Applied Biology & Pharmaceutical Technology, Oct - Dec -2011; 2(4).
59. Pankaj Nainwal, Deepak Nanda, Amandeep Singh, D. A. Jain, FORMULATION AND EVALUATION OF SOLID DISPERSION OF ROSUVASTATIN WITH VARIOUS CARRIERS,Pharmacie Globale International Journal Of Comprehensive Pharmacy, Issn 0976-8157.
60. Pankaj Nainwal, Amandeep Singh1, Deepak Nanda, D.A.Jain, SOLUBILITY ENHANCEMENT OF AN ANTIHYPERLIPIDEMIC DRUG ROSUVASTATIN BY SOLID DISPERSION TECHNIQUE, International Journal of PharmTech Research IJPRIF ISSN: 0974-4304, March-June 2012; 2: 3.

61. Kshitiz Agrawal, Pragati Bailwal, Amandeep Singh. Prem Saini, DEVELOPMENT OF QUALITY STANDARDS OF SUPRABHATAM CHURNA: A POLY HERBAL FORMULATION, International Journal of Pharmaceutical Research & Development,IJPRD, 2011; 4, June 2012.
62. Kapil Kalra, Amandeep Singh, Manisha Gaur, Ravindra P. Singh, and D. A. Jain, ENHANCEMENT OF BIOAVAILABLITY OF RIFAPENTINE BY SOLID DISPERSION TECHNIQUE, International Journal Of Pharmacy & Life Sciences, Kalra et al., April, 2011; 2(4).
63. Pankaj nainwal, Ranveer batsa, Amandeep singh, Deepak nanda, MEDICINAL PLANT STUDIES INFLUECED BY THE BIOTECHNOLOGICAL METHODS: A UPDATED REVIEW, International Journal of Pharma and Bio Sciences Apr-June-2011; 2(2).
64. Amandeep Singh, Sandhiya Pal, Prem Saini, IN- VITRO EVALUTION OF ANTI-INFLAMMATOTRY ACTIVITY OF TERMANALIA ARJUNA BARK EXTRACT, Journal of Innovative trends in Pharmaceutical Sciences,Vol-1(1): 9-12.
65. Amandeep Singh, Pramila Chauhan, Prem Saini, IN-VITRO ANTI-INFLAMMATORY EVALUTION OF HYDROALCOHALIC LEAVES EXTACT OF PINUS ROXBURGHII BY HRBC METHOD, International journal of Research in Pharmaceutical and Nano Sciences, 2013; 2(3): 268-271.
66. Amandeep Singh, Sumit Negi, Prem Saini, In Vitro Anti-Inflammatory Evaluation Of Leaves Using Hydroalcohalic Extract Of “Mangifera indica” International Journal of Pharmacy and Integrated Life Sciences, V1-(I7) PG (93-98).
67. Aman Deep Baghla, Kshitij Agarwal, Ramesh Verma and Deepak Nanda, Wound Healing Effect of the Aqueous Extract of the Leaves of Psidium guajava Linn., International Journal of chemicals and Life Sciences, 2013; 02 (03): 1104-1106.
68. Aman Deep Baghla, Kshitij Agarwal, Ramesh Verma and Deepak Nanda, WOUND HEALING EFFECT OF THE AQUEOUS EXTRACT OF THE LEAVES OF PSIDIUM GUAJAVA LINN., International Journal of chemicals and Life Sciences, 2013; 02(03): 1104-1106.
69. Bhupendra Kumar, Meenakshi Ghildiyal, Yogesh Tiwari, Deepika Chauhan, Amandeep Singh, IN-VITRO ANTI-INFLAMMATORY ACTIVITY OF GLYCINE MAX SEEDS, Indo American Journal Of Pharmaceutical Sciences, 2018; 05(02): 868-871.
70. Piyali Dey, Jyoti Pandey, Bhupendra kumar, Amandeep Singh, IN VITRO ANTHELMINTIC ACTIVITY OF BARK EXTRACTS OF ARTOCARPUS HETEROPHYLLUS, International Journal of Pharmacy & Pharmaceutical Research, 2018; 03(11): 33-40.
71. Bhupendra Kumar, Yogesh Tiwari, Amandeep Singh, Vineet Kumar, IN VITRO ANTIUROLITHIC ACTIVITY OF FICUS PALMATA LEAVES, International Journal Of Pharmaceutical Technology And Biotechnology, 2019; 6(1): 01-09.
72. Md. Daneyal Khurshid, Vivek Shukla, Bhupendra Kumar and Amandeep A Review Paper on Medicinal Properties of Phyllanthus emblica, International Journal of Pharmacy and Biological Sciences, 2020; 10(3): 102-109.
73. Mr. Dwivedi Vishal, Mrs. Nisha A Bhatt, Dr. Amandeep Singh PREPARATION AND STANDARDIZATION OF NAVKARSHIKA CHURNA, World Journal of Pharmacy and Pharmaceutical Sciences, 2020; 9(8).
74. Mitun Saha1, Mr. Bhupendra Kumar, Dr. Amandeep Singh Review Article on Various Phytochemicals and Different Medicinal Activities of Haritaki International Journal of Innovative Science and Research Technology, June 2020; 5(6).