

## Research Article

# Efficacy of a Retinoid, Kera- tolytic, Anti-Inflammatory and Antibacterial Gel and Spray Formulations in Mild Common Acne

Massimo Milani<sup>1\*</sup>, Lola Casas Gonzales<sup>2</sup> and Maria Villalba<sup>2</sup>

<sup>1</sup>Medical Affair, Cantabria Labs Difa Cooper, Caronno P, Italy

<sup>2</sup>Medical Affair, Cantabria Labs, Madrid, Spain

### Abstract

**Background and Objectives:** For the treatment of mild/moderate acne, topical retinoids and antibacterial molecules are used in monotherapy or in combination. An exfoliating and anti-inflammatory action can increase the clinical efficacy of this therapeutic approach. A topical product in Gel and Spray Formulations (GF and SF) with retinoids (hydroxypinacolone retinoate and encapsulated retinol), with anti-inflammatory (niacinamide), antibacterial (biopep15) and keratolytic (glycolic and salicylic acids) activity has recently been developed. Topical retinoids have anti-inflammatory, anti-seborrheic and anticomedone-formation properties. Biopep15 is an oligopeptide with antibacterial action that can interfere with lipoteichoic acid, a component of the wall of *Cutibacterium acnes*. In addition, Biopep15 can perform also an antagonistic action against the Toll-Like-Receptor 2, involved in the pathogenesis of acne. Niacinamide has a well-known anti-inflammatory action. Salicylic and glycolic explain keratolytic and exfoliating activities. In this study the objective was to determine the efficacy and tolerability of GF and SF in mild/moderate comedogenic acne.

**Methods:** In a 4-week, open-label, prospective trial, 32 patients between the ages of 15 and 30 have been evaluated. All participants gave their written consent. Treatment with gel (for facial lesions) and spray (for lesions located on thorax, back and shoulder) applied twice daily were used. To assess clinical efficacy, a count of comedogenic lesions (open and closed comedones; non-inflammatory lesions: NIL) and inflammatory lesions (IL; papules, and pustules) was performed and the reduction in the number of lesions after 2 and 4 weeks of treatment was evaluated. An evaluation of Total le-

sions count (TL; NIL+IL) was also performed. The lesion count data were analysed with a paired Student's t test. We evaluated also the exfoliating/keratolytic activity and the effect on sebum production assessed at baseline, after 2 and 4 weeks of treatment. Finally, to evaluate *Cutibacterium acnes* (*C. acnes*) skin colonization, we performed a fluorescence detection of skin porphyrin content at baseline and at day 28, by mean of Visiopor PP 34 camera.

**Results:** All patients completed the trial. At baseline the NIL, IL and TL count were 14.3, 8.7 and 23, respectively. After 2 weeks of GF/SF treatment, NIL, IL and TL significantly decreased to 9.7 (-32%), 6.8 (-22%) and 16.5 (-29%), respectively. At the end of the treatment, a significant reduction in comparison with baseline was observed for NIL (-49%) IL (-63%) and TL (-54%). The exfoliating index evaluated in comparison with baseline value improved not significantly by 13% at day 14, and significantly ( $p=0.05$ ) by 18% at day 24. The *Cutibacterium acnes* skin colonization area was significantly ( $p=0.02$ ) reduced by 28% in comparison with baseline. Treatment was well tolerated, and local tolerability was assessed as optimal by all patients.

**Conclusion:** This new anti-acne combination formula based on retinoids, antibacterial oligopeptide, keratolytic and anti-inflammatory agents have shown high clinical efficacy and good tolerability in patients with mild to moderate acne. The treatment shows also a keratolytic effect and a significant reduction of *C. acnes* skin colonization.

**Keywords:** Acne; Clinical trial; Niacinamide; Topical retinoids

### Introduction

Acne is a very common inflammatory skin disease affecting skin area rich in sebaceous glands, like face, thorax, shoulder and back [1]. Acne is mainly a disease of the pilosebaceous unit [2]. Hyperseborrhea, hyperkeratinisation, *Cutibacterium acnes* proliferation and inflammation are the four very well-known acne pathogenetic factors [3]. Specific anti-acne treatments should address ideally all these factors. For the treatment of mild/moderate acne, topical retinoids and antibacterial molecules are used in monotherapy or in combination [4]. Retinoid molecules, used orally or topically, are very effective in normalizing keratinocyte differentiation and proliferation therefore reducing the initial acne lesions (comedones) [5]. Anti-bacterial compound can reduce the presence of pathogenetic population of *C. acnes* [6]. An exfoliating and anti-inflammatory action can increase the clinical efficacy of this therapeutic approach. A topical product in gel and spray formulations (GF/SF) (BiretixTriactive®, Cantabria Labs, Madrid, Spain) with retinoids (hydroxy pinacolone retinoate and retinol encapsulated with glycospheres), with anti-inflammatory (niacinamide), antibacterial (biopep15) and keratolytic (glycolic and salicylic) activity has recently been developed. The gel formulation is used for acne lesions located on the face; the spray formulation is commonly used to treat large skin surfaces. The gel formulation of this product has already demonstrated to be efficacious and well tolerated in the treatment of common acne [7]. Topical retinoids have anti-inflammatory, anti-seborrheic and anticomedone formation properties [8]. Biopep15 is an oligopeptide with antibacterial action that can interfere with lipoteichoic acid, a component of the wall of *Cutibacterium acnes* [9]. In addition, Biopep15 can perform also an antagonistic

\*Corresponding author: Massimo Milani, Department of Medical Affair, Cantabria Labs Difa Cooper, Via Milano 160, Caronno P, Italy, Email: massimo.milani@difacooper.com

**Citation:** Milani M, Gonzales LC, Villalba M (2021) Efficacy of a Retinoid, Keratolytic, Anti-Inflammatory and Antibacterial Gel and spray Formulations in Mild Common Acne. J Clin Dermatol Ther 7: 089.

**Received:** October 22, 2021; **Accepted:** October 28, 2021; **Published:** November 04, 2021

**Copyright:** © 2021 Milani M, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

action against the Toll-Like-Receptor 2, involved in the pathogenesis of acne and in the inflammatory process involved in acne lesion formation [10]. Niacinamide has a relevant anti-inflammatory action [11]. Salicylic and glycolic exert exfoliating activity [12]. Therefore, the composition of this innovative topical formulation could act against all the factors involved in the pathogenesis of common acne. Furthermore, the product is vehiculated as both a gel and a spray. The latter formulation could be a convenient topical composition for the treatment not only of the face but also for other area involved in the development of acne lesions such as thorax, shoulders, and the back [13].

## Study Aim

To assess the clinical efficacy and tolerability of GF/SF in mild/moderate comedogenic acne.

## Study Design

We conducted a 4-week, open-label, prospective trial, in subjects with mild-to-moderate acne.

## Methods

The trial, conducted by Zurko Bioresearch CRO Company (Madrid Spain), was performed between January 2018 and March 2018.

## Subjects

We have enrolled thirty-two subjects. All participants gave their written consent. Main inclusion criteria were, both sexes, aged between 15 and 30 years with mild to moderate common acne (<100 comedon lesions, <50 inflammatory lesions, no more than 2 nodules). Main exclusion criteria were severe form of acne, pregnancy or breast-feeding, other clinically relevant skin diseases other than acne. Treatment with GF/SF (twice application per day on average depending on the extension of the affected area) was used in the most affected skin localization (GF for face; SF for back, chest and shoulders).

## Study Outcomes

To assess clinical efficacy, a count of comedonic lesions (non-inflammatory lesions: NIL) and inflammatory lesions (IL; papules and pustules) was performed and the reduction in the number of lesions at 2 (day 14) and 4 weeks (day 28) of treatment was evaluated. Macro high-definition face pictures were performed for each enrolled subject at baseline and at day 28. An evaluation of Total lesions count (TL=NIL+IL) was also performed. We have also evaluated the exfoliating/keratolytic activity by mean of Corneofix F 20 (Courage+Khazaka GmbH) and the effect on sebum production evaluated by means of sebometer (SebuFix F16; Courage+Khazaka GmbH) and the assessed at baseline, after 2 and 4 weeks of treatment. To evaluate P. acnes skin colonization, we performed a fluorescence detection of skin porphyrin content at baseline and at day 28. The skin porphyrin content was determined by Visiopor PP 34 camera (Courage+Khazaka, Cologne, Germany), which uses a specific UVA light (375 nm) with a measured area of 6 × 8 mm. The porphyrins are visible as fluorescent orange-red spots in the pores, which indicate the presence of P. acnes within and on the surface of the follicular impactions or comedones. The parameters analysed were the number and percentage of the area covered by orange-red spots.

## Statistical Analysis

Statistical analysis was performed using GraphPad statistical software ver. 13.0 (La Jolla, CA, USA). Continuous variables were expressed as mean±SD. The primary endpoint of the trial was the evolution of acne lesions from baseline today 14 and day 28 (end of treatment). The Wilcoxon and the ANOVA tests were used for the analysis of the study outcomes (lesion count, corneometry, sebometry and porphyrin detection).

## Results

All patients completed the trial. Treatment was well tolerated, and local tolerability was assessed as optimal by all patients.

### Clinical efficacy on acne lesions

At baseline the number of NIL was 14.2±2.6 and the number of IL was 8.7±2.5 with a TL mean number of 23±3. The product induced a significant ( $p = 0.0001$ ) reduction of NIL, IL and TL at both 14 and 28 days. NIL lesion count was reduced by 32% at day 14 and by 54% at day 28. IL were reduced by 22% at day 14 and by 63% at day 28. The TL count was reduced by 29% at day 14 and by 54% at day 28. Figure 1 summarizes the evolution of acne lesions (NIL, IL and TL) from baseline and after 14 and 28 days of treatment. Treatment was well tolerated, and local tolerability was assessed as optimal by all patients. Figure 2 shows the pictures of three subjects at baseline and after 28 days of treatment.

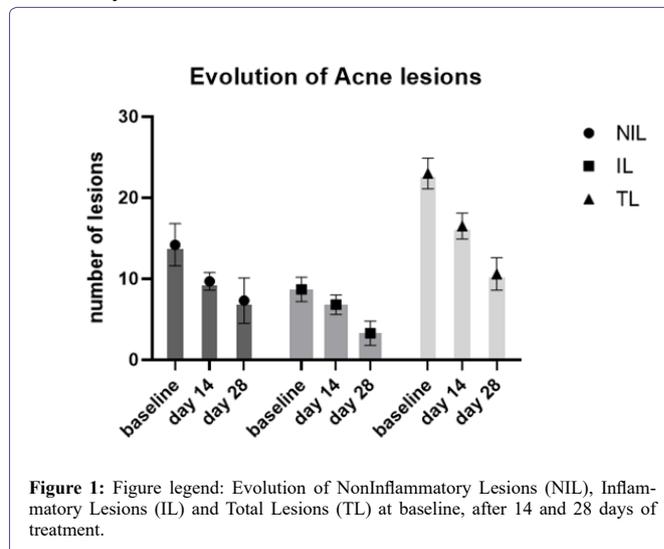


Figure 1: Figure legend: Evolution of NonInflammatory Lesions (NIL), Inflammatory Lesions (IL) and Total Lesions (TL) at baseline, after 14 and 28 days of treatment.

### Exfoliating keratolytic effect

The exfoliating index evaluated in comparison with baseline value (mean value 5.1±1.9) improved not significantly by 13% at day 14, and significantly ( $p=0.05$ ) by 18% at day 24.

### Sebum production

The instrumental evaluation of seborrhea did not show significant differences between baseline value and after treatment. However, during treatment 38% (day 14) and 57% of subjects (day 28) presented an improved of seborrhea (reduction of area covered by sebum) in comparison with baseline.

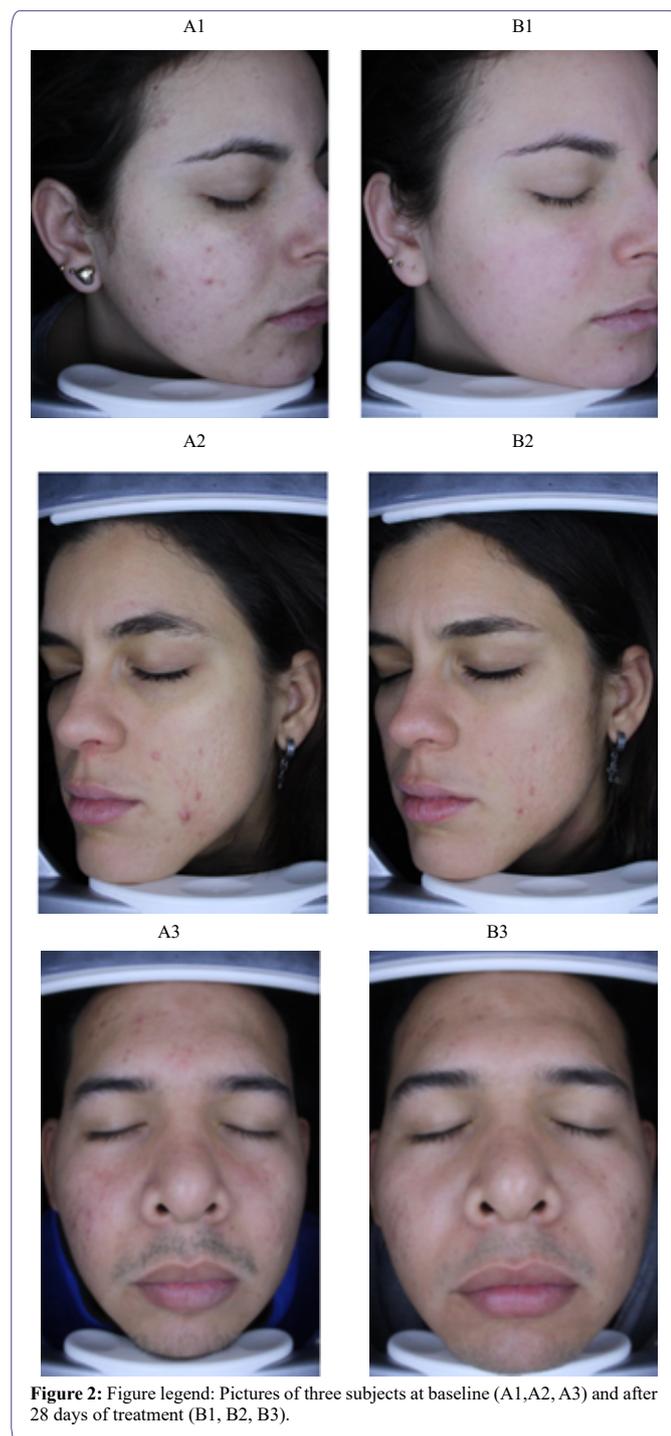


Figure 2: Figure legend: Pictures of three subjects at baseline (A1,A2, A3) and after 28 days of treatment (B1, B2, B3).

### C. acnes colonization: Porphyrin fluorescence detection

The use of the Visiopor PP34 camera at baseline and at day 28 showed that the intensity and the extension of fluorescence area were significantly ( $p=0.02$ ) reduced by 28% in comparison with baseline. An improvement (i.e., reduction) in area covered by positive fluorescence was documented in 25 out of 32 subjects (76%).

### Discussion

In this trial we demonstrated that a topical product in gel and spray formulation containing retinoid, keratolytic, anti-inflammatory and

antibacterial compound is effective and well tolerated as monotherapy in subjects with mild to moderate common acne inducing a significant reduction in non-inflammatory and inflammatory acne lesions. In this trial we have also demonstrated that the product has also a significant keratolytic action and a direct anti *P. acnes* activity, supported by the data of porphyrin fluorescence. These two topical formulations contain retinoids, anti-inflammatory molecule (niacinamide) an antibacterial (biopep15) and finally two components (glycolic and salicylic) with keratolytic activity. Therefore, it could exert positive anti-acne actions toward all the relevant pathophysiology processes involved in the formation of acne lesions (comedo formation, seborrhea, inflammation, *P. acnes* proliferation). The clinical efficacy in term of percentage reduction of acne lesions is in line with the results of other topical drug products [14,15].

A relevant aspect to underline is the good skin tolerability of this formulation even if it contains retinoids and keratolytic agents. Topical retinoids are considered as first line therapy in mild and moderate acne [16]. However, especially during the very first days of therapy a low local skin tolerability could limit their use [17]. In this product the retinoid component (mainly hydroxypinacolone retinoate) is characterized by a tolerability profile better than other retinoid compounds [18,19]. In addition, the presence in the formulation of niacinamide amide, an anti-inflammatory molecule [20], could at least in part explain the good tolerability profile of the tested product. In evaluating the results of our study, we must consider some trial's limitations. This was uncontrolled, not randomized trial. However, to improve the internal validity of the present study we performed instrumental evaluations such as corneometry, sebum production and porphyrin fluorescence evaluation. All these instrumental evaluations were in line with the clinical improvement regarding the evolution of acne lesions observed in the study.

### Conclusion

This new anti-acne formula based on retinoids, antibacterial oligopeptide, keratolytic and anti-inflammatory agents have shown high clinical efficacy and good tolerability in patients with mild to moderate acne. The product reduces also significantly the colonization of the skin by *P. acnes*.

### Statement of Ethics

The study was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The subjects have given their written informed consent to publish their case including the images used in this article).

### Study approval Statement

Ethics approval was obtained.

### Consent to Publish Statement

Written informed consent was obtained from participants and in one case by legal guardians for publication of the details of their medical case and used images.

### Conflict of Interest Statement

M.M., LC and MV are employees of Cantabria Labs group.

## Funding Sources

This trial was funded by Cantabria Labs Difa Cooper.

## Author Contributions

MM, LC and MV participate in the writing of the final manuscript and data analysis.

## Data Availability Statement

Source data are available upon specific request.

## References

1. Mahto A (2017) Acne vulgaris. *Medicine* 45: 386-389.
2. Williams HC, Dellavalle RP, Garner S (2012) Acne vulgaris. *The Lancet* 379: 361-372.
3. Dagnelie MA, Corvec S, Khammari A, Dréno B (2021) Update on Cutibacterium acnes. In *Acne*, Springer, Cham, Page no: 1-15.
4. Thielitz A, Gollnick H (2008) Topical retinoids in acne vulgaris. *Am J Clin Dermatol* 9: 369-381.
5. Krautheim A, Gollnick HP (2004) Acne: topical treatment. *Clinics in Dermatology* 22: 398-407.
6. Graber EM (2021) Treating acne with the tetracycline class of antibiotics: A review. *Dermatological Reviews*.
7. Villani A, Annunziata MC, Cinelli E, Donnarumma M, Milani M, et al. (2020) Efficacy and safety of a new topical gel formulation containing retinol encapsulated in glycospheres and hydroxypinacolone retinoate, an antimicrobial peptide, salicylic acid, glycolic acid and niacinamide for the treatment of mild acne: preliminary results of a 2-month prospective study. *G Ital Dermatol Venereol* 155: 676-679.
8. dos Santos Marubayashi BA, Simoni SE, de Fariña LO (2021) Topical treatments for acne: a bibliographic review. *Brazilian Journal of Health Review* 4: 3910-3922.
9. Gabriel MTG, Oblepias MSM, Vitale M (2020) Safety and Efficacy of Retinsphere® Technology and Biopep-15 in the treatment of Acne in Asian Population. *J Clin Cosmet Dermatol* 4.
10. Lotz S, Aga E, Wilde I, Van Zandbergen G, Hartung T, et al. (2004) Highly purified lipoteichoic acid activates neutrophil granulocytes and delays their spontaneous apoptosis via CD14 and TLR2. *J Leukoc Biol* 75: 467-477.
11. Gehring W (2004). Nicotinic acid/niacinamide and the skin. *J Cosmet Dermatol* 3: 88-93.
12. Merinville E, Laloef A, Moran G, Jalby O, Rawlings AV (2009) Exfoliation for sensitive skin with neutralized salicylic acid? *International Journal of Cosmetic Science* 31: 243-244.
13. Sheth AH, Sen DJ, Doshi NB (2011) New Researches on Acne Vulgaris. *Research Journal of Pharmacology and Pharmacodynamics* 3: 48-57.
14. Mcginley KJ, Webster GF, Leyden JJ (1980) Facial follicular porphyrin fluorescence: correlation with age and density of Propionibacterium acnes. *Br J Dermatol* 102: 437-441.
15. Gollnick H, Schramm M (1998) Topical therapy in acne. *J Eur Acad Dermatol Venereol* 11: 8-12.
16. Gollnick HP, Krautheim A (2003) Topical treatment in acne: current status and future aspects. *Dermatology* 206: 29-36.
17. Mukherjee S, Date A, Patravale V, Korting HC, Roeder A, et al. (2006) Retinoids in the treatment of skin aging: an overview of clinical efficacy and safety. *Clin Interv Aging* 1: 327-328.
18. Veraldi S, Barbareschi M, Guanziroli E, Bettoli V, Minghetti S, et al. (2015). Treatment of mild to moderate acne with a fixed combination of hydroxypinacolone retinoate, retinol glycospheres and papain glycospheres. *G Ital Dermatol Venereol* 150: 143-147.
19. Bettoli V, Zauli S, Borghi A, Toni G, Ricci M, et al. (2016) Efficacy and safety of a 12-month treatment with a combination of hydroxypinacolone retinoate and retinol glycospheres as maintenance therapy in acne patients after oral isotretinoin. *Giornale italiano di dermatologia e venereologia: organo ufficiale. G Ital Dermatol Venereol* 152: 13-17.
20. Wohlrab J, Kreft D (2014) Niacinamide - mechanisms of action and its topical use in dermatology. *Skin Pharmacol Physiol* 27: 311-315.



- Advances In Industrial Biotechnology | ISSN: 2639-5665
- Advances In Microbiology Research | ISSN: 2689-694X
- Archives Of Surgery And Surgical Education | ISSN: 2689-3126
- Archives Of Urology
- Archives Of Zoological Studies | ISSN: 2640-7779
- Current Trends Medical And Biological Engineering
- International Journal Of Case Reports And Therapeutic Studies | ISSN: 2689-310X
- Journal Of Addiction & Addictive Disorders | ISSN: 2578-7276
- Journal Of Agronomy & Agricultural Science | ISSN: 2689-8292
- Journal Of AIDS Clinical Research & STDs | ISSN: 2572-7370
- Journal Of Alcoholism Drug Abuse & Substance Dependence | ISSN: 2572-9594
- Journal Of Allergy Disorders & Therapy | ISSN: 2470-749X
- Journal Of Alternative Complementary & Integrative Medicine | ISSN: 2470-7562
- Journal Of Alzheimers & Neurodegenerative Diseases | ISSN: 2572-9608
- Journal Of Anesthesia & Clinical Care | ISSN: 2378-8879
- Journal Of Angiology & Vascular Surgery | ISSN: 2572-7397
- Journal Of Animal Research & Veterinary Science | ISSN: 2639-3751
- Journal Of Aquaculture & Fisheries | ISSN: 2576-5523
- Journal Of Atmospheric & Earth Sciences | ISSN: 2689-8780
- Journal Of Biotech Research & Biochemistry
- Journal Of Brain & Neuroscience Research
- Journal Of Cancer Biology & Treatment | ISSN: 2470-7546
- Journal Of Cardiology Study & Research | ISSN: 2640-768X
- Journal Of Cell Biology & Cell Metabolism | ISSN: 2381-1943
- Journal Of Clinical Dermatology & Therapy | ISSN: 2378-8771
- Journal Of Clinical Immunology & Immunotherapy | ISSN: 2378-8844
- Journal Of Clinical Studies & Medical Case Reports | ISSN: 2378-8801
- Journal Of Community Medicine & Public Health Care | ISSN: 2381-1978
- Journal Of Cytology & Tissue Biology | ISSN: 2378-9107
- Journal Of Dairy Research & Technology | ISSN: 2688-9315
- Journal Of Dentistry Oral Health & Cosmesis | ISSN: 2473-6783
- Journal Of Diabetes & Metabolic Disorders | ISSN: 2381-201X
- Journal Of Emergency Medicine Trauma & Surgical Care | ISSN: 2378-8798
- Journal Of Environmental Science Current Research | ISSN: 2643-5020
- Journal Of Food Science & Nutrition | ISSN: 2470-1076
- Journal Of Forensic Legal & Investigative Sciences | ISSN: 2473-733X
- Journal Of Gastroenterology & Hepatology Research | ISSN: 2574-2566
- Journal Of Genetics & Genomic Sciences | ISSN: 2574-2485
- Journal Of Gerontology & Geriatric Medicine | ISSN: 2381-8662
- Journal Of Hematology Blood Transfusion & Disorders | ISSN: 2572-2999
- Journal Of Hospice & Palliative Medical Care
- Journal Of Human Endocrinology | ISSN: 2572-9640
- Journal Of Infectious & Non Infectious Diseases | ISSN: 2381-8654
- Journal Of Internal Medicine & Primary Healthcare | ISSN: 2574-2493
- Journal Of Light & Laser Current Trends
- Journal Of Medicine Study & Research | ISSN: 2639-5657
- Journal Of Modern Chemical Sciences
- Journal Of Nanotechnology Nanomedicine & Nanobiotechnology | ISSN: 2381-2044
- Journal Of Neonatology & Clinical Pediatrics | ISSN: 2378-878X
- Journal Of Nephrology & Renal Therapy | ISSN: 2473-7313
- Journal Of Non Invasive Vascular Investigation | ISSN: 2572-7400
- Journal Of Nuclear Medicine Radiology & Radiation Therapy | ISSN: 2572-7419
- Journal Of Obesity & Weight Loss | ISSN: 2473-7372
- Journal Of Ophthalmology & Clinical Research | ISSN: 2378-8887
- Journal Of Orthopedic Research & Physiotherapy | ISSN: 2381-2052
- Journal Of Otolaryngology Head & Neck Surgery | ISSN: 2573-010X
- Journal Of Pathology Clinical & Medical Research
- Journal Of Pharmacology Pharmaceuticals & Pharmacovigilance | ISSN: 2639-5649
- Journal Of Physical Medicine Rehabilitation & Disabilities | ISSN: 2381-8670
- Journal Of Plant Science Current Research | ISSN: 2639-3743
- Journal Of Practical & Professional Nursing | ISSN: 2639-5681
- Journal Of Protein Research & Bioinformatics
- Journal Of Psychiatry Depression & Anxiety | ISSN: 2573-0150
- Journal Of Pulmonary Medicine & Respiratory Research | ISSN: 2573-0177
- Journal Of Reproductive Medicine Gynaecology & Obstetrics | ISSN: 2574-2574
- Journal Of Stem Cells Research Development & Therapy | ISSN: 2381-2060
- Journal Of Surgery Current Trends & Innovations | ISSN: 2578-7284
- Journal Of Toxicology Current Research | ISSN: 2639-3735
- Journal Of Translational Science And Research
- Journal Of Vaccines Research & Vaccination | ISSN: 2573-0193
- Journal Of Virology & Antivirals
- Sports Medicine And Injury Care Journal | ISSN: 2689-8829
- Trends In Anatomy & Physiology | ISSN: 2640-7752

Submit Your Manuscript: <https://www.heraldopenaccess.us/submit-manuscript>