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Sun Protection Factor, Antioxidant, and in Silico Study of Some Synthesized Benzylidene Analogues of Ketamine Against Elastase and Collagenase

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Keywords:
Ketamine.
Sun Protection.
Collagenase.
Elastase.
Antioxidants.

ABSTRACT

Background: The degradation of ozone layer is in part due to human activities, climate change. These have led to many skin diseases. Scientists are investigating for new alternative sun protection agents having low toxicity. Therefore, analogues of ketamine (benzylidenes) were investigated for sun protection ability. Objective: In this present research work, derivatives of ketamine synthesized from the department of Pharmaceutical and Medicinal Chemistry Niger Delta Uniersity Bayelsa state (D11-D15) were experimented for sun protection factor. Also, antioxidant and in vitro anti-elastase and anti-collagenase activities and in silico studies were carried out **Methods**: in vitro spectrophotometric determination of derivatives of ketamine were carried out, DPPH antiradical scavenging ability of D11-D15, total antioxidant capacity and ferric reducing antioxidant power were also evaluated on the compounds (D11-D15). Also in vitro spectrophotometric assays on anti-elastase and anti-collagenase were also carried out on (D11-D12) and lastly molecuar docking studies were carried out on (D11-D12) against the enzymes elastase and collagenase. **Results**: The results from the study revealed that D11-D15 at concentrations of 25, 50 and 100 µg/ml shows higher SPF values. Also, the total antioxidant capacity reported as microgram ascorbic acid equivalent/g compound shows that D14 > D11 > D13 > D12 > D15. Also, the DPPH radical scavenging potentials and ferric reducing antioxidant power reported as percentages and microgram gallic acid equivalent/g compound revealed higher values. The anti-elastase and anti-collagenase targeted with ketamine analogues showed that (D11-D15) inhibited elastase and collagenase activity results presented as IC50; these results were confirmed by the docking studies as the analogues bind more tightly to the active sites of elastase and collagenase better than sivelestat and acetylcysteine respectively. Conclusion: Our result shows that D11-D15 could serve as sun protection agents, antioxidants and antiaging especially in the cosmetic industry.

عامل الحماية من أشعة الشمس، مضادات الأكسدة ودراسة حاسوبية لبعض نظائر البنزيلدين المركبة من الكيتامين ضد الإيلاستاز والكولاجيناز

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الملخص

الاساس النظري: يعود تدهور طبقة الأوزون جزئياً إلى الأنشطة البشرية وتغير المناخ. وقد أدى ذلك إلى ظهور العديد من الأمراض الجلدية. يعكف العلماء على البحث عن عوامل حماية جديدة بديلة من أشعة الشمس ذات سمية منخفضة. لذلك، تمت دراسة نظائر الكيتامين (البنزيلدين) من حيث قدرتها على الحماية من أشعة الشمس، ومضادات الأكسدة، ومضادات الإيلاستاز والكولاجيناز في دراسات مختبرية وحاسوبية. الهدف: في هذا البحث، تم اختبار مشتقات الكيتامين المركبة من قسم الكيمياء الصيدلانية والطبية بجامعة دلتا النيجر بولاية بايلسا (D11 الى D15) من حيث عامل الحماية من أشعة الشمس. كما تم إجراء دراسات على الأنشطة المضادة للأكسدة والمضادة للإيلاستاز والكولاجيناز في المختبر وفي الحاسوب. **الطرق:** تم إجراء تحديد طيفي ضوئي لمشتقات الكيتامين في المختبر، كما تم تقييم قدرة (D11 الى D15) على إزالة الجذور الحرة DPPH، والقدرة المضادة للأكسدة الكلية، وقوة مضادات الأكسدة المختزلة للحديد على المركبات (D11 الى D15). كما تم إجراء اختبارات طيفية ضوئية في المختبر على مضادات الإيلاستاز والكولاجيناز على (D11-D12) وأخيرًا تم إجراء دراسات ربط جزيئي على (D11 الىD12) ضد إنزيمات الإيلاستاز والكولاجيناز. **النتائج:** أظهرت نتائج الدراسة أن D11-D15 بتركيزات 25 و50 و100 µg/ml تظهر قيم SPF أعلى. كما أظهرت السعة المضادة للأكسدة الإجمالية المبلغ عنها بالميكروغرام من حمض الأسكوربيك المكافئ/غرام من المركب أن D14> D11 > D13 > D12 > D15. كما أظهرت إمكانات إزالة جذور DPPH والقدرة المضادة للأكسدة المختزلة للحديد المبلغ عنها بالنسب المئوية والميكروغرام من حمض الغاليك المكافئ/غرام من المركب, قيمًا أعلى. أظهرت مضادات الإيلاستاز والكولاجيناز المستهدفة بنظائر الكيتامين أن (D11 الى D15) تثبط نشاط الإيلاستاز والكولاجيناز، كما هو موضح في IC50؛ وقد تم تأكيد هذه النتائج من خلال دراسات (docking)، حيث ترتبط النظائر بشكل أقوى بالمواقع النشطة للإيلاستاز والكولاجيناز بشكل أفضل من السيفليستات والأسيتيل سيستين على التوالي. الاستنتاج: تظهر نتائجنا أن D11 الىD15 يمكن أن تعمل كعوامل حماية من أشعة الشمس ومضادات للأكسدة ومضادات للشيخوخة خاصة في صناعة مستحضرات التجميل.

الكلمات المفتاحية:

الكيتامين.

الحماية من أشعة الشمس.

الكولاجيناز.

الإيلاستاز.

مضادات الأكسدة.

1. Introduction

Human activities centered on chlorofluorocarbons and many other activities have negatively damaged the ozone layer. Also, excessive exposure of the skin to ultra-violet light due to outdoor entertainment or other outdoor activities leads to many health problems [1-3].

Skin is the protective cover of our whole body, is constantly exposed to the environment, making it prone to environmental damage leading to aging [4]. The aging skin is due to external and internal factors. Internal factors induced skin aging arises because of metabolism in the skin cells which produced free radicals. Production of radicals in excess from the skin leads to wrinkle formation. This is due to the activation of the extracellular membrane enzyme collagenase and elastase [5]. External factors inducing skin aging included environmental pollution, irradiation and xenobiotic. This can also lead to the production of many free radicals in the skin [6,7]. The breakdown of elastin and collagen [fibrous proteins that supports the skin extracellular matrix] by elastase and collagenase are activated by reactive oxygen species [5]. Collagen a structural protein made of three polypeptides wounds around itself is found in skin, tendon, bone, cartilage and teeth [8]. Therefore, the hydrolysis of collagen and elastin induced by free radicals triggers the onset of wrinkling and aging in the skin [9]. Collagenase and elastase the enzymes that degrade collagen and elastin during the chronological and photo aging, leading to sagging, coarse, laxity and wrinkling of the skin belongs to a matrix metalloproteinase family of proteins, that are transmembrane [8].

Sunlight consists of ultraviolet [UV] radiation, which can be beneficial or harmful to the skin. Ultraviolet radiation wavelength ranges from 200-280 nm known as UV-C, 280-320 nm UV-B and 320-400 as UV-A [10]. Little exposure to sunlight is useful for vitamin D formation [11]. Excessive exposure to sunlight is carcinogenic, it also give rise to other effects like depression of the immune system, sunburn, and accelerated skin aging [12]. Prolonged UV exposure can lead to the production of free radicals in the tissues of the skin. These radicals damage macromolecules like protein, DNA, and lipids. These radicals and damaged macromolecules lead to overproduction of oxidants in the skin cells [oxidative stress]. Oxidative stress can lead to harmful effects such as inflammation, aging and skin cancer [13]. A natural pigment in our skin is melanin. Melanin produced in the epidermis protects skin from the adverse effects of UV radiation. However prolonged exposure of melanin to UV can cause age spots, melisma and other skin problems [14]. Therefore, to protect the skin sunscreens are needed containing UV filters. Filters can absorb or reflect UV radiation, by decreasing its penetration into the skin. However, many synthetic UV filters are toxic [15]. Many strategies employed to inhibit skin aging is to reduce the activity of metalloproteinase enzymes elastase and collagenase. Benzylidenes derived from ketamine shown chemically below were synthesized at the Department of Pharmaceutical Chemistry in the faculty of Pharmacy, Niger Delta University, Bayelsa State. These Ketamine analogues [Benzylidenes] were used as sun protection factor, antioxidant and anti-collagenase and elastase activity *in vitro* and *in silico* in this present study. In the literature there are no works carried out utilizing analogues of ketamine against skin aging in vitro and *in silico*. Therefore, the present study was to determine *in vitro* sun protection of some benzylidene analogues of ketamine.

Ketamine is used medically for the induction and maintenance of anesthesia, it is also used for the treatment of depression and pain management [16]. Its action is on the N-methyl D-aspartic acid receptor [NMDA] [17]. Ketamine antagonistic ability on NMDA receptors can provide analgesia, but cannot induce complete loss of consciousness [18]. Ketamine has local anesthetic effects by interacting with receptors like the opioid receptors, monoamine, cholinergic, purinergic and adrenoreceptors [17]. Organic plant extract with sun protection factors also faces some limitation due to rigorous, time consuming process and micro yields of active compound. Titanium oxide and zinc oxide are widely used as sun protection agents but they are prone to corrosion, thereby decreasing their usage [19]. Also, organic sun protection agents are due to aromatic ring linked to a carbonyl group e.g para-aminobenzoic acid and benzophenones [20]. Chalcones with α,β unsaturated bonds and aromaticity absorbs UV light [21,22]. Therefore, all the derivatives of ketamine synthesized in the department of Pharmaceutical and Medicinal Chemistry possesses chalcone-like properties of benzene

ring and α,β unsaturated bonds. Therefore, the present study was designed to evaluate the *in vitro* sun protection of some benzylidene analogues of ketamine, due to their easy or possible production.

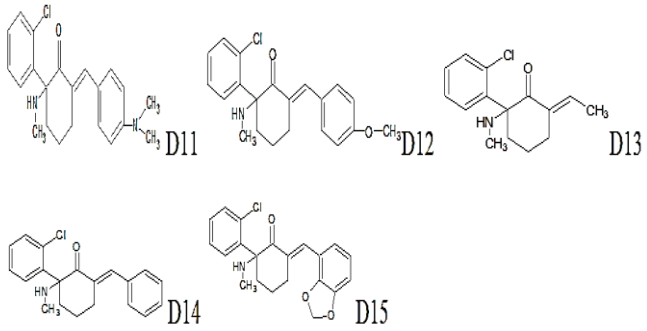

Fig. 1: Different ketamine derivatives

ketamine derivatives [D11 to D15] was synthesized in Pharmaceutical and Medicinal chemistry Department in which the name of every compound as: D11: -2-[2-chlorophenyl]-6-[[4-dimethylaminophenyl]methylidene]-2-[methylamino]cyclohexan-1-one, D12: 2-[2-chlorophenyl]-6-[[4-methoxyphenyl]methylidene]-2-[methylamino]cyclohexan-1-one, D13: 2-[2-chlorophenyl]-6-[[4-methoxyphenyl]methylidene]-2-[methylamino]cyclohexan-1-one, D14: 6-benzylidene-2-[2-chlorophenyl]-2-[methylamino]cyclohexan-1-one, D15:]-6-[[2*H*-1,3-benzodioxol-4-yl]methylidene]-2-[2-chlorophenyl]-2-[methylamino]cyclohexan-1-one.

2. Materials and Methods

2.1 Chemicals

DMSO, sulfuric acid, sodium phosphate, ammonium molybdate, DPPH, ethanol, TPTZ, sodium acetate trihydrate, 2,4,6 tripyridyl-s-triazine, hydrochloric acid, $FeCl_3.6H_2O$, sodium chloride, calcium chloride, collagenase from bacteria *Clostridium histolyticum* 0.8 units/mL, N-[3-[2-furyl] acrylonyl]. Leu-Gly-Pro-Ala, tricine buffer, bovine serum albumin, glucose, sodium hydrogen phosphate, sodium dihydrogen phosphate, acetylcysteine, sivelestat, ketamine derivatives [D11-D15], N-succinyl-Ala-Ala-p-nitroanitide pancreatic elastase.

2.2 Stock Solutions of Benzylidene Analogues

Each compound D11-D15 was weighed out [0.5g] and dissolved in 50 ml DMSO. These solutions were used for antioxidant assays, sun protection factor and anti-elastase and collagenase assay.

2.3 Determination of Sun Protection Factor *in vitro*

Different concentrations of D_{11} – D_{15} at 25, 50 and 100 µg/ml were scanned through 290 – 320 nm at 5 nm increments of wavelength. DMSO was used as blank solvent. The results were calculated based on the mathematical equation of Mansur et al [23].

2.4 Antioxidant assays

Total Antioxidant Assay

The method of Prieto [24] and colleagues was utilized for total antioxidant capacity of ketamine analogues. Each compound D_{11}-D_{15} [0.1ml] was added to the reagent consisting of sulfuric acid 0.6 M, sodium phosphate 28 mM and ammonium molybdate 4mM. All tubes were incubated at 95º C in a water bath for 90 minutes. Afterwards the samples were transferred to an ice -containing compartment, and later cooled. The absorbance of all tubes were read at 695 nm. Total antioxidant capacity was expressed as µg AAE/g compound. Ascorbic acid was used as a reference compound.

2.5 DPPH Radical Scavenging Activity

Ability of D_{11} – D_{15} to act as anti-radical was evaluated by the method described by Braca et al [25]. DPPH ethanolic solution [0.05 mM] 0.3 ml was mixed with 1 ml of D_{11} – D_{15}. The mixture was incubated at room temperature in dark for 30 min. absorbance was determined at 517 nm and ascorbic acid served as reference and results were calculated as percentage inhibition.

2.6 Ferric Reducing Antioxidant Power [FRAP]

The reduction of Fe^{3+} -tetra [2-pyridyl] pyrazine [TPTZ] to Fe^{2+} -tripyridyltriazine at low pH as explained by Benzie and Strain [26] was utilized. FRAP reagent made of sodium acetate buffer 300 mM pH 3.6, 10 mM TPTZ in 40 mM HCl and 20 mM ferric chloride in a ratio of [10:1:1 v/v/v]. The ketamine analogues D_{11} – D_{15} were dissolve in DMSO and 30 µL of FRAP working solution was added in triplicate tubes and D_{11} – D_{15} compounds were also added 500 µL. The reaction mixture was incubated for 8 min and absorbance read at 593 nm. Gallic acid served as reference drug. Results were expressed as µg GAE/g benzylidene.

2.7Anti-elastase activity

The method of Kim et al [27] was adopted for in vitro elastase assay. The enzyme elastase solution was prepared in distilled water and N-succinyl-Ala-P-nitroanilide [AAAPVN] was prepared in buffer as substrate. The concentrations of D_{11}-D_{15} used were 0-100 µg/ml and were incubated with the enzyme for a time period of 15min before the addition of elastase's substrate AAAPVN of 0.8 mM. Absorbance was measured at 400nm using a spectrophotometer. Analysis were done in triplicate and percentage inhibition was calculated [% inhibition] and result presented in percentages.

2.8 Collagenase inhibitory activity

Kim et al [27] explained method was adopted. Tricine buffer was prepared 50mm and 400mm NaCl and 10mm $CaCl_2$ was included pH 7.5. This serves as solvent for dissolving the enzyme collagenase obtained from clostridium histolyticum. When the enzyme was dissolved in tricine buffer it concentration was 0.8 units/ml. Also a 0.002 M solution of substrate N-[3-[2-furyl] acryloyl]-Leu-Gly-Pro-Ala in tricine was prepared. The benzulidenes D11-D15 were prepared in DMSO at concentrations of 0-100 µg/ml and the reference drug acetyl cysteine. The reaction mixture was incubated in the presence of enzyme, substrate, with or without benzylidenes for 15min and absorbance was taken at 490nm. The percentage collagenase inhibition was represented as $1C_{50}$.

2.9Molecular docking of elastase and collagenase

Molecular modeling and docking of the binding protein and ketamine analogs [ligands] were done using the Maestro software of OPLS3, 2018 Force field and Pymol software [28,29]. The crystal structure of *Pseudomonas aeruginosa* elastase protein complexed with N-alpha-l-rhamnopyranosyloxy[hydroxyphosphinyl]-l-leucyl-l-tryptophan [PBD: 3DBK], and the crystal Structure of Collagenase G from *Clostridium histolyticum* in complex with Isoamylphosphonyl-Gly-Pro-Ala at 3.25, angstrom resolution protein [PDB: 2Y6I] was obtained from the protein data bank [PDB] website and used for the molecular docking studies. Sivelestat was used as the control standard 3DBK, while acetylcysteine for 2Y6I, respectively.

2.10 Statistical analysis

All results were computed utilizing excel software, results were reported as mean ± S.D. $P<0.05$ was also obtained through one-way analysis of variance using GraphPad prism software.

3.Results

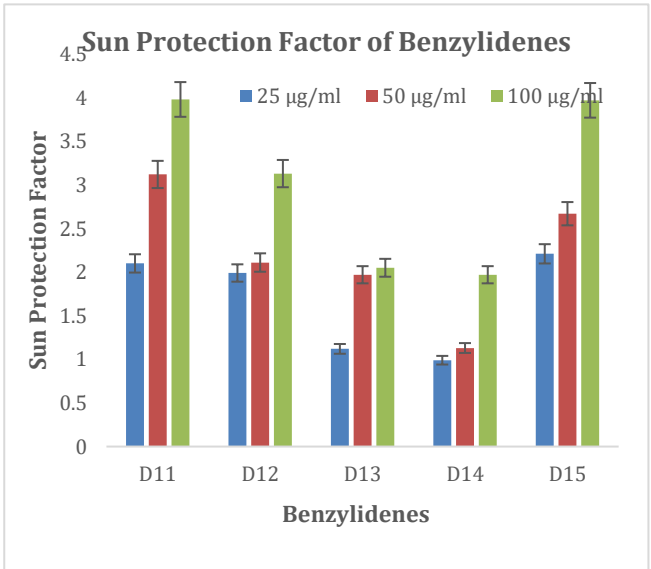

Fig. 2: Depicts sun protection factor of benzylidenes D_{11}-D_{15}. Values are mean ±S.D [n=3]. D_{11}, D_{15} and D_{12} showed the highest SPF at 100 µg/ml concentration respectively

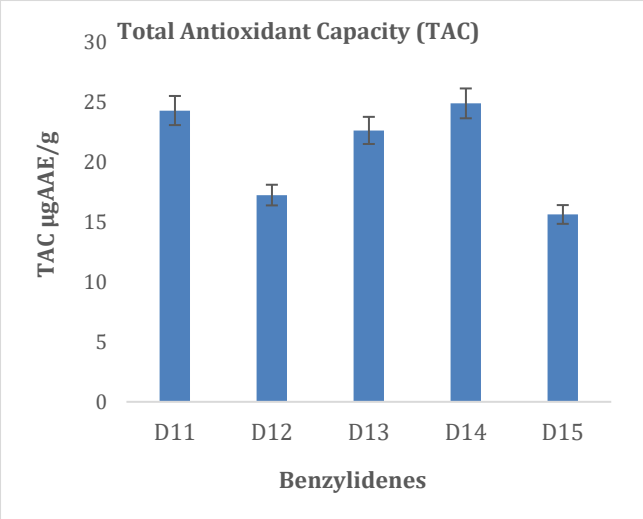

Fig. 3: Depicts total antioxidant capacity of benzylidenes D_{11}-D_{15} represented as µg AAE/g. Values are mean ±S.D [n=3]. D_{14}, D_{11} and D_{13} showed higher TAC.

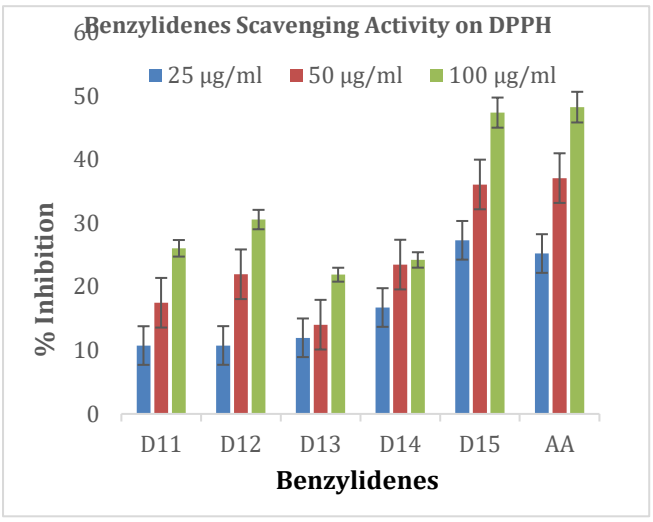

Fig. 4: Depicts DPPH radical scavenging ability of benzylidenes D_{11}-D_{15} represented as percentages. Values are mean ±S.D [n=3]. D_{15} and ascorbic acid [AA] showed higher percentages of inhibition at 25, 50 and 100 µg/ml.

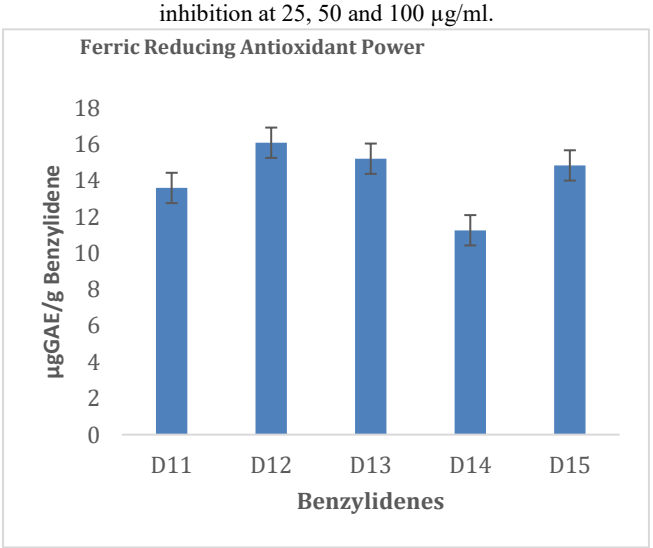

Fig. 5: Depicts ferric reducing antioxidant power of benzylidenes D_{11}-D_{15} represented as µgGAE/g. Values are mean ±S.D [n=3]. D_{12} and D_{13} showed higher FRAP values.

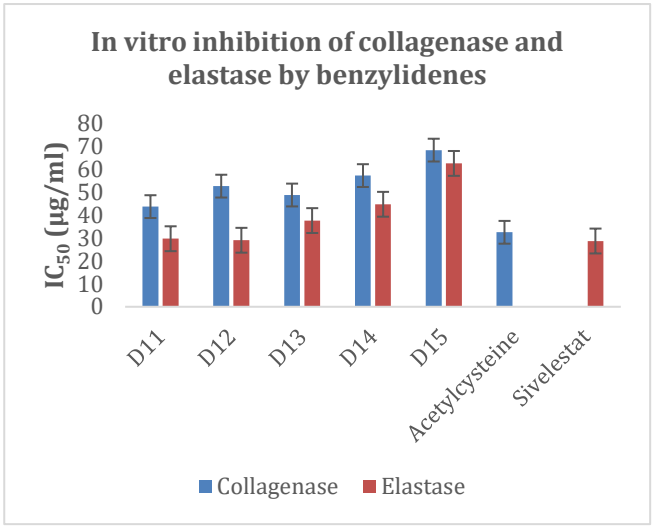

Fig. 6: Depicts inhibitory concentration at 50 % of benzylidenes D_{11}-D_{15} represented as IC_{50} [µg/ml]. Values are mean ±S.D [n=3]. $D_{11}$and D_{12} showed better IC_{50} as does the standard drug acetylcysteine and sivelestat.

The results of the present study are presented as bar charts, tables and docking poses

Table 1: Molecular docking scores of D11-D15, silvelestat and acetyl cysteine

Compound ID	PDB ID: 3DBK		PDB ID: 2Y6I	
	Docking Score [kcal/mol]	Glide emodel	Docking Score [kcal/mol]	Glide emodel
D11	-5.20	-48.80	-4.56	-35.41
D12	-4.33	-50.27	-4.48	-33.68
D13	-4.78	-43.15	-4.45	-34.70
D14	-4.11	-46.35	-4.04	-35.91
D15	-4.10	-45.44	-4.22	-43.82
Sivelestat [Std]	-3.52	-44.30	—	—
Acetyl Cysteine [Std]	—	—	-3.05	-20.94

std – standard, NB: the lower the docking score, the better the ligand binding affinity, i.e., -5.20>-4.78>4.33>4.11, etc

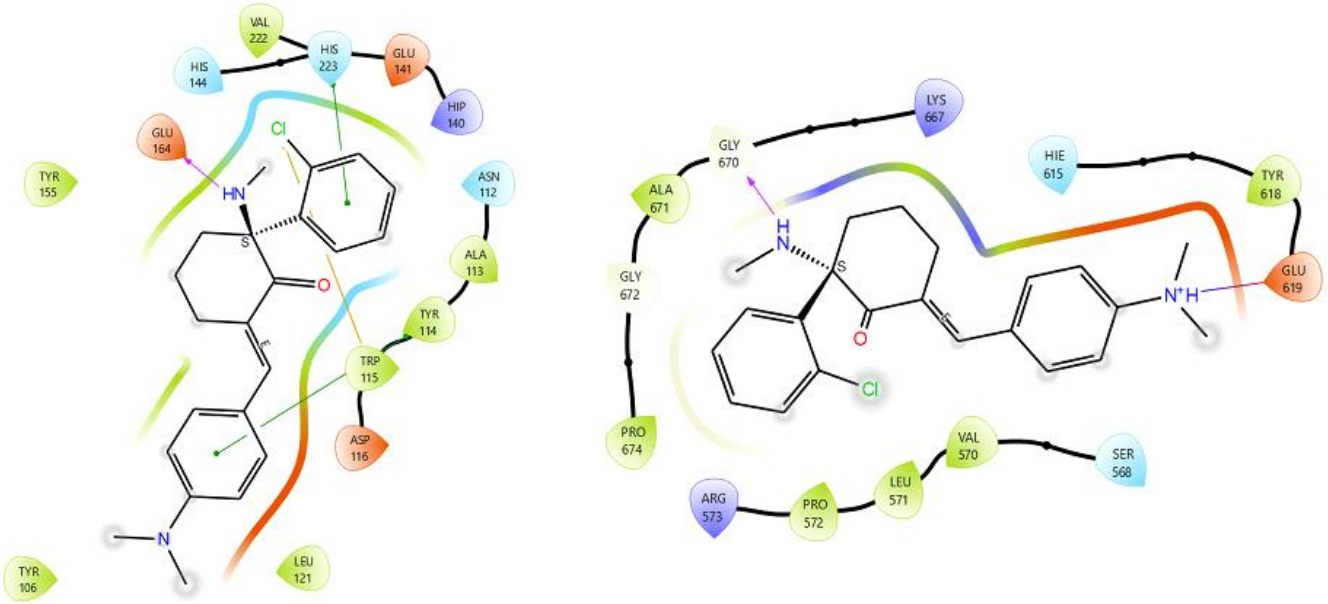

Fig. 7: Molecular docking poses of elastase [3DBK] left or collagenase [26YI] right against D11

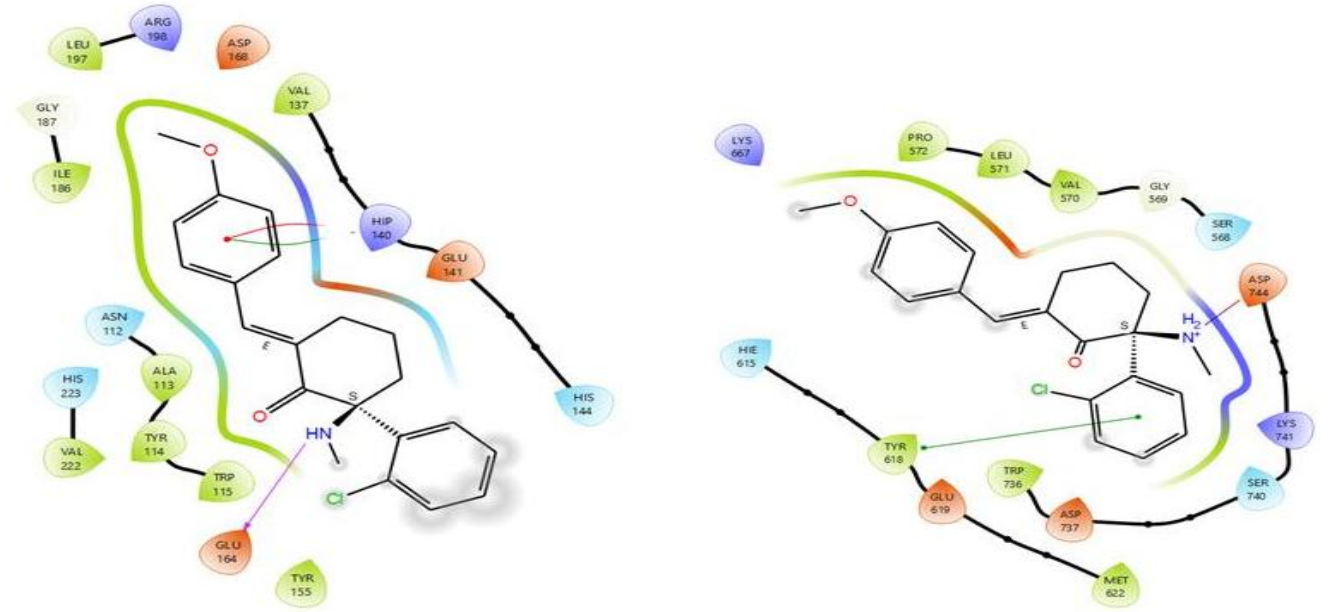

Fig. 8: Molecular docking poses of elastase [3DBK] left or collagenase [26YI] right against D12

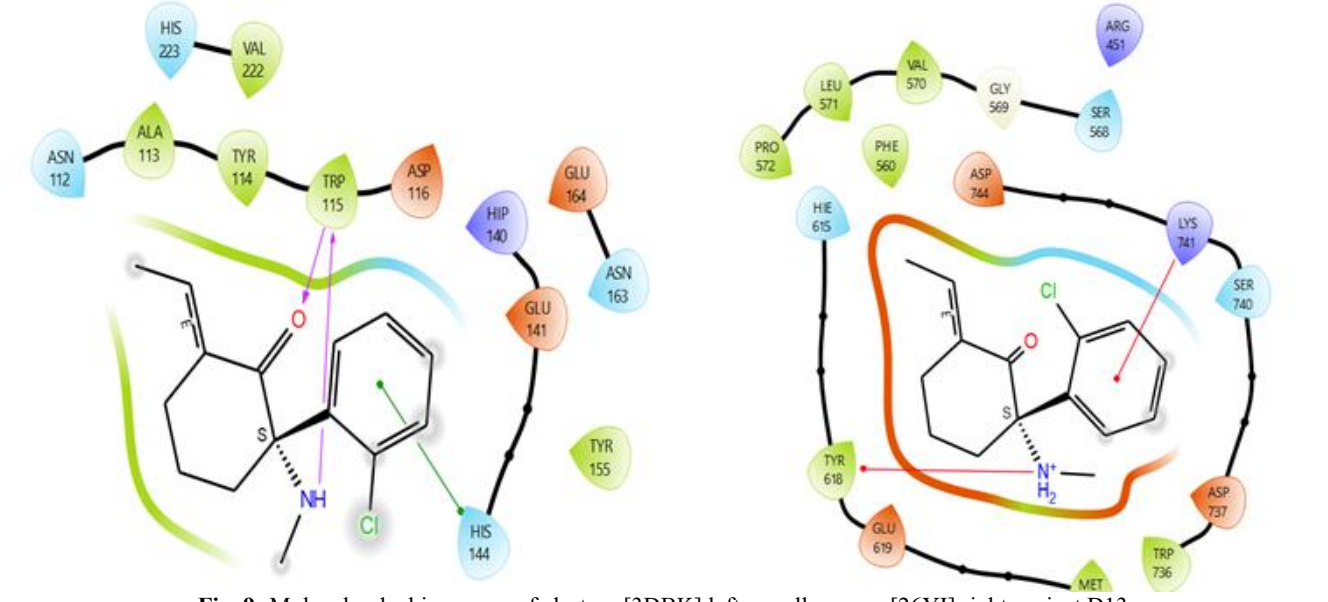

Fig. 9: Molecular docking poses of elastase [3DBK] left or collagenase [26YI] right against D13

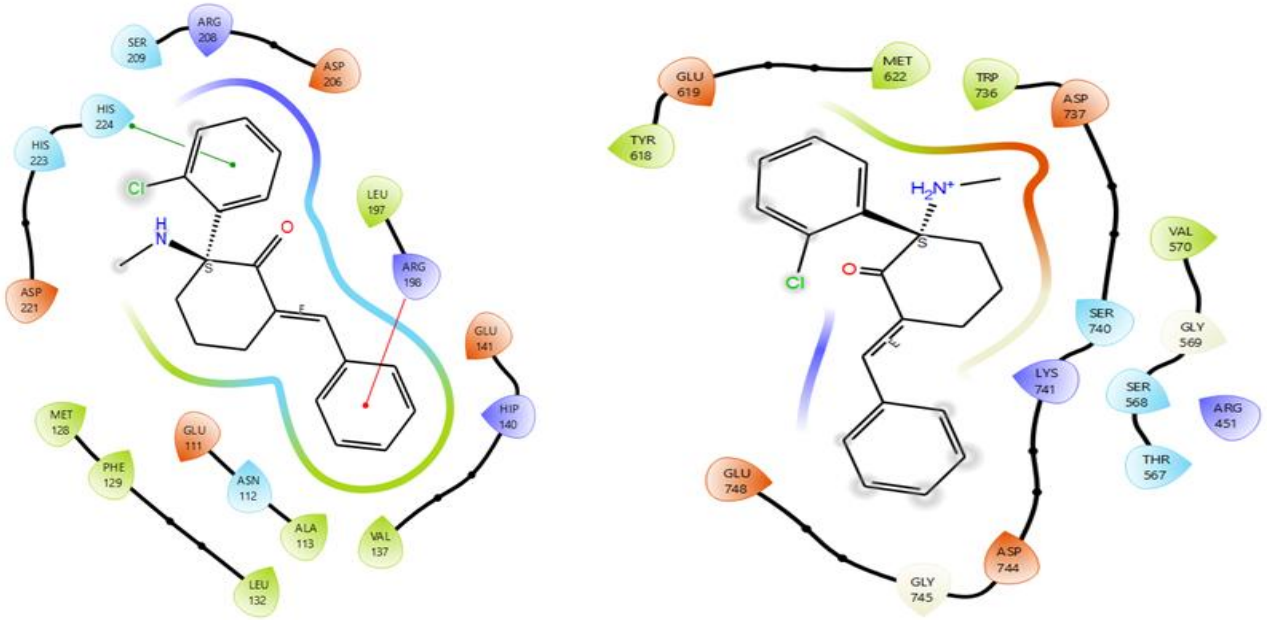

Fig. 10: Molecular docking poses of elastase [3DBK] left or collagenase [26YI] right against D14

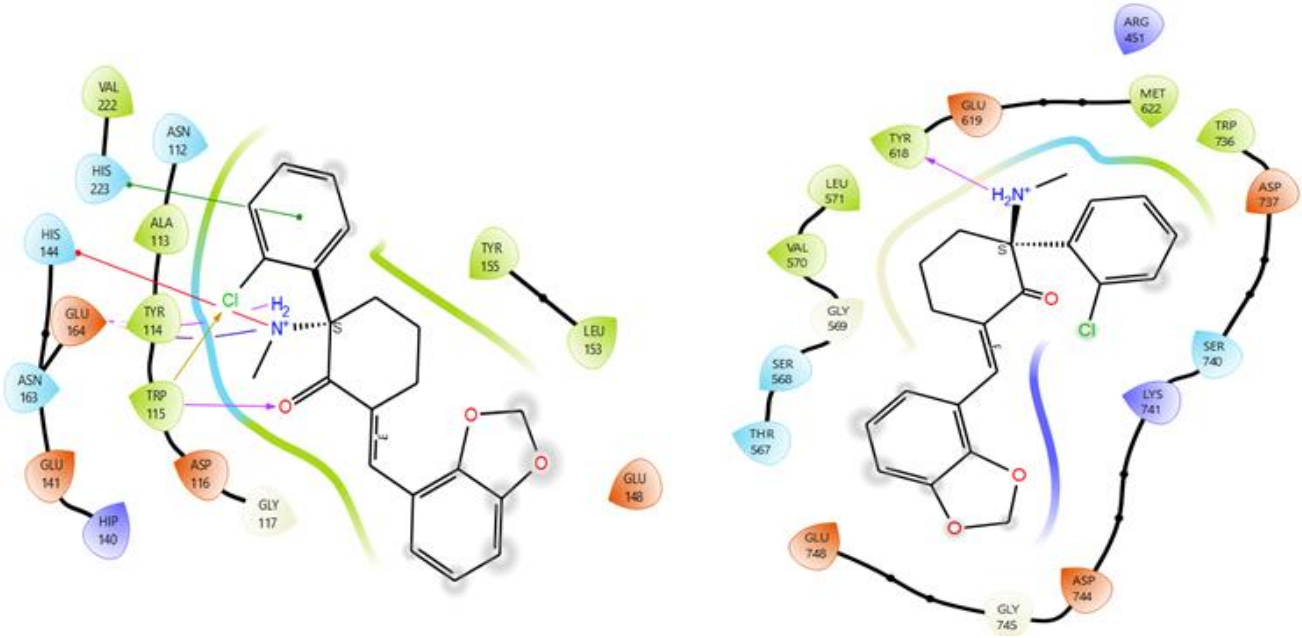

Fig. 11 Molecular docking poses of elastase [3DBK] left or collagenase [26YI] right against D15

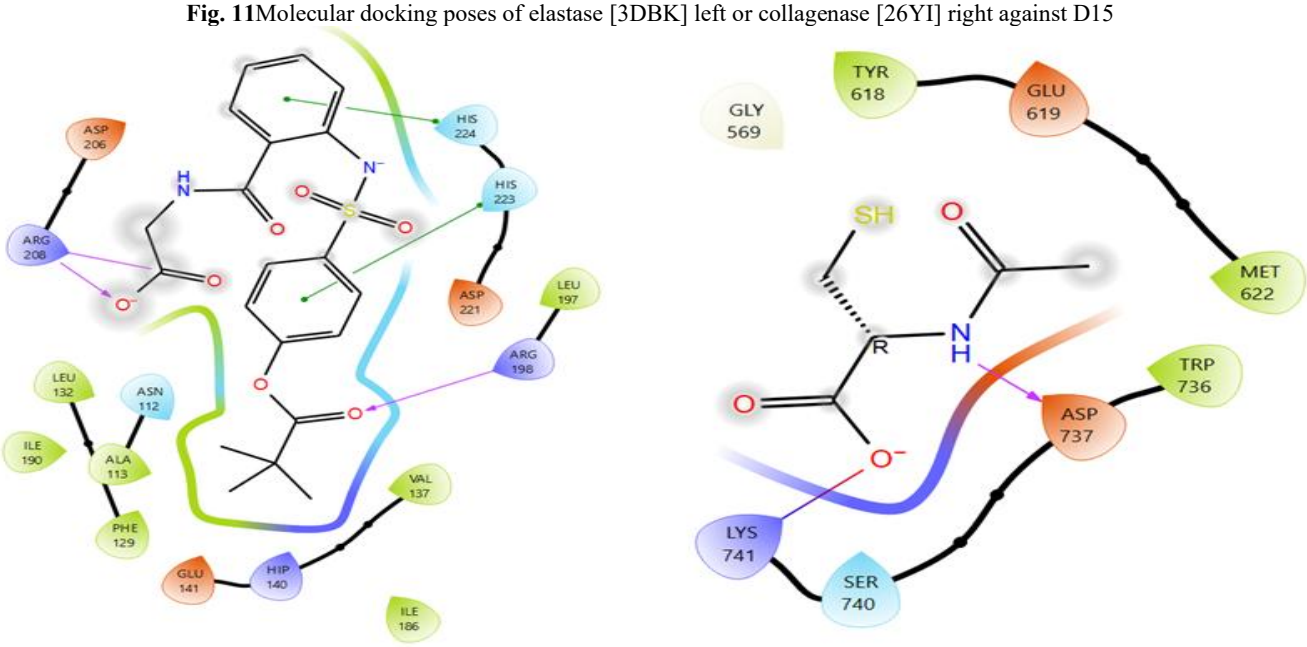

Fig. 12: Molecular docking poses of elastase [3DBK] left or collagenase [26YI] right against sivelestat and acetyl cysteine respectively

4. DISCUSSION

The radiation from the sun affects the skin, because it is the biggest external organ, it contains chromophores like melanin, DNA, RNA, proteins and water. The photochemical reaction that arises leads to the production of reactive oxygen species [30]. The destructive action of ROS to the skin can be prevented by vitamins, carotenoids and enzymatic antioxidants [31]. The rays of the sun that reaches the earth is nearly 50% visible light, 40% infrared and 10% UV radiation [32]. UV radiation pierces deeper into the skin and therefore leads to many skin disorders. Therefore, there is the need to look for safer synthetic drugs to retard the dangerous effects of the sun's rays. In the present study the sun protection factor of the different benzylidenes examined showed appreciable levels of SPF as depicted in fig 2. The results are similar to the works of Maske et al [33] and Poh-Yen et al [34].

Leopoldin et al [35] asserted that mechanism of action of antioxidant is based on hydrogen or electron transfer and metal chelation. The total antioxidant of benzylidene was carried out by the phosphomolybdate method and the results depicted in fig 3. The mechanism behind this assay was the addition of an electron to Mo [VI] to form Mo [V] by benzylidenes and thereby acting as antioxidants. Our work reveals that the total antioxidant of the benzylidenes were high in D14> D11> D13> D12> D15. These results are in line with the reports of Dasgupta and De 2004 [36]; Batool et al [37] who reported total antioxidant capacity of *Piper betle* leaf and *Brachychiton populneus* leaves respectively.

The degree of decolorization of DPPH is exhibited by antioxidants [38]. The antioxidant potentials of D_{11}-D_{15} were evaluated by total antioxidant capacity, DPPH radical scavenging and FRAP assays. DPPH absorbs maximally at 517nm, the decrease in its absorbance indicated that benzylidenes have transferred an electron to the radical, thereby acting as antioxidant. The results of DPPH radical scavenging by benzylidenes indicated that D_{15}>D_{14}>D_{13}>D_{12}>D_{11} respectively. This is due to the ring structure of the derivatives of ketamine acting as resonance stable structures due to the abstraction of a radical. These results are in agreement with the works of Gupta et al [39] who reported DPPH scavenging activity of 3-Substituted-2-Oxindole Derivatives.

The Ketamine analogues labelled D_{11}-D_{15} acted as antioxidants based on the fact that substances, that can reduce Ferric-TPTZ complex into bluish ferrous TPTZ complex are considered antioxidants [40] . The present results of the FRAP assay were reported as µgGAE/g Benzylidenes. The mechanism of action of the derivatives of ketamine having higher FRAP values is that the structures can accommodate an electron and become stable. The results revealed that the FRAP value of D_{12}>D_{13}>D_{15}>D_{11}>D_{14} as depicted in fig 5 these result followed the same pattern as reported by Gupta et al [39]; Perera et al [41] and Sre et al [38].

Elasticity of the skin is maintained by the collagen found in the extracellular matrix. The intact collagen can be destroyed by ROS and metalloproteinases activity such as those of collagenase and elastase [41]. Elastin like collagen is also found on the ECM of organs and connective tissues, thereby increasing the elasticity of the skin. Elastase is a metalloproteinase enzyme that destroys elastin in the skin. The catalyzing of both collagen and elastin into smaller peptides leads to skin wrinkles, aging and hyperpigmentation. Therefore, inhibition of their activity is useful in the cosmetic industry [27,5]. The present study showed that benzylidenes inhibited elastase more compared to the inhibition of collagenase which is similar to the in silico studies. Therefore, our reports are similar to the research studies of Thring et al and Abdelfattah et al [42,43]; Matos et al [5] and Elgamal et al [4].

The 2D interaction of D_{11} structure and the binding site of elastase show a slightly better binding score of -5.20kcal/mol as compared to the standard inhibitor -3.52 kcal/mol sivelestat. This was due to the presence of H-bonding on His 223, Glu 164 and Trp 115 and the chloride and benzene ring. D_{11} uses its amide hydrogen to interact tightly through H-bonding on Gly 670 and Glu 619 also in the active site of collagenase affording it a binding score of -4.56 kcal/mol as compared to -3.05 kcal/mol of acetyl cysteine. D_{12} with a -4.33 kcal/mol also displays better binding interaction in the active site of elastase as Glu 164 and HIP 140 H-bond and hydrophobically interact with D_{12} respectively. D_{12} and collagenase interact tightly according to the 2D docking model displayed showing hydrophobic interaction between Tyr 618 and D_{12} and Asp 744 interacting with positively charged amide group of D_{12} ionically giving rise to -4.48 kcal/mol. D_{13} donate H-bond to Trp 115 in the active site of elastase and also uses its ketone group on cyclohexane in the structure to accept H-bond from Trp115. There is also a hydrophobic interaction between His144 and D_{13}. D_{13} ionically bind to Tyr 618 utilizing its charged [positive] amine group. also there was a pi-pi-H-bonding between Lys 241 and D_{13}. This is why the binding score of D_{13} and collagenase was -4.45 kcal/mol. D_{14} interacts with elastase via hydrophobic interaction with His 224. Also Arg 198 aslo interact with D_{14} through Pi-cationic interaction on the benzene ring. D_{14} and the active site of collagenase show no visible interaction. The active site of elastase fits with the chemical structure of D_{15} as there was hydrophobicity between His 223 and D15. Also an ionic bonding between His 144 and D_{15}, H-bonding between Glu 164 and the amide group of D_{15}. Also Trp 115 makes H-bonding to D_{15} as well as a halogen bond to D_{15}. There is only one H-bond between Tyr 618 in the active site of collagenase and D_{15} only. In all these the binding scores of the ketamine analogues are better than the standard sivelestat and acetylcysteine. Our reports are in line with similar works of Matos et al [5]; Elgamal et al [4] and Abdelfattah et al [43].

5. Conclusion

Our results revealed that benzylidenes derived from ketamine possess sun protective ability as it is revealed by their high SPF values. They also possess antioxidant properties because in the DPPH radical scavenging, total antioxidant capacity and ferric reducing antioxidant power assays they are better antioxidant molecules. These analogues also have anti-aging potential based on the *in vitro* spectrophotometric studies and the molecular docking studies. Therefore, these compounds are very useful in the cosmetic industry.

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7. References

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