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## **Long chain aliphatic hydroxy ketones isolated from biological active plant sources during last 50 Years**

Chandan Prasad<sup>1</sup>, Vimal Kumar<sup>3\*</sup>, H.S. Pandey<sup>2</sup>, R. M. Srivastava<sup>1</sup>, Kamal Kumar<sup>5</sup> and R. B. Srivastava<sup>4</sup>

<sup>1</sup>Department of Chemistry, D.A.V. P.G. College, Kanpur -208001, Uttar Pradesh, India

<sup>2</sup>Department of Chemistry, Buddha P.G. College, Kushi Nagar-274403, Uttar Pradesh, India

<sup>3</sup>Science Laboratory, Archaeological Survey of India, Dehradun-248001, Uttarakhand, India

<sup>4</sup>Defence Institute of High Altitude Research, c/o 56 APO - 901205, India

<sup>5</sup>Defence Materials and Stores Research and Development Establishment, Kanpur- 208013, Uttar Pradesh, India

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### **ABSTRACT**

Over the years, the biological activities of medicinal plants and their compounds have gained considerable research interest due to their specific functional compounds, The novel long chain aliphatic hydroxyl ketones reported from medicinal plants over the past years are increasingly being recognized as new active compounds. The extraction of such active compounds has also attracted special attention recent years. Potent biologically active long chain aliphatic hydroxy ketones, from medicinal plants have been shown to play significant role towards prevention of degenerative diseases such as cancer, inflammation, arthritis, diabetes, parkinson's disease, alzheimer's disease, and certain other neurodegenerative disorders. The novel chemical entities derived from medicinal plants as active components for can be used in many industrial applications such as functional foods, pharmaceuticals and nutraceuticals. This review intends to explore such thirty eight long chain aliphatic hydroxy ketones isolated from twenty one different medicinal plants during last fifty years (1960 – 2010) for their possible application as anticancer, antimicrobial and antioxidant activities.

**Keywords:** Hydroxy ketones, Anticancer, Antimicrobial, Antioxidant

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### **INTRODUCTION**

A perusal of history of human civilization clearly indicate that for thousands of years of early human existence man has largely relied on natural products as principal source of food, medicines and materials for shelter. Many scientific and philosophic concepts related to ancient system of medicines have been compiled in 'Ayurveda' of India, 'Pun-Tea' of China, 'Ebera papyrus' of Egypt, 'History of Plants' of Greeks, 'Destmplicibus' of Rome and the 'Arabic Herbal' of Arabs. Even today, these literature sources continue to serve as useful clues for several useful drugs. One of the earliest treatises of Indian medicine, the Charaka Samhita (1000 B.C.) mentions the use of over 2000 herbs for medicinal purposes [1]. Bioactive compounds from such plants have been compounds produced by plants having pharmacological or toxicological effects towards man and animals. These characteristic bioactive compounds in plants are produced as secondary metabolites and are classified according

to different criteria. An approach based on biological effects is complicated by the fact that the clinical outcome has not always been exclusively connected to chemically closely related compounds; even chemically very different molecules might produce similar clinical effects [2].

**Objective of the study:** In the present review, we have carried out an in-depth literature survey on the isolated long chain aliphatic hydroxy ketones from twenty one different plants along with their ethno pharmacological applications during last fifty years (1960 – 2010).

### **RESULTS AND DISCUSSIONS**

**Ketones and their applications:** Ketones were first discovered in urine of diabetic patients in mid-19<sup>th</sup> century. In 1920s, a drastic "hyperketogenic" diet was found remarkably effective for treatment of drug-resistant epilepsy in children. In 1967, circulating ketones were discovered to replace

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\*Corresponding Author Address: Dr. Vimal Kumar, Archaeological chemist, Science Laboratory, Archaeological Survey of India, 29 new cantt road, Dehradun-248001, Uttarakhand, India. Email: vimal\_drl@yahoo.in

glucose as the brain's major fuel during the marked hyperketonemia of prolonged fasting. Until then, the adult human brain was thought to be entirely dependent on glucose. During the 1990s, diet induced hyperketonemia was found therapeutically effective for treatment of several rare genetic disorders involving impaired neuronal utilization of glucose or its metabolic products. Finally, growing evidence suggests that mitochondrial dysfunction and reduced bioenergetic efficiency occur in brains of patients with Parkinson's disease (PD) and Alzheimer's disease (AD). Because ketones are efficiently used by mitochondria for ATP generation and may also help to protect vulnerable neurons from free radical damage, hyperketogenic diets should be evaluated for ability to benefit patients with PD, AD, and certain other neurodegenerative disorders [3]. The carbonyl group (C=O) is found in ketones. The carbon in the carbonyl group is sp<sup>2</sup>-hybridized, with bond angles of 120°. In ketones, two carbon groups are attached to the carbonyl carbon ketones therefore they have boiling points that are in between those of alcohols and hydrocarbons of the same molecular weight. Ketones are polar, so they have higher boiling points than hydrocarbons, but they are not as polar as molecules which can bond hydrogen. Low-molecular weight ketones are water-soluble and water solubility decreases as the size of the molecule increases. Secondary alcohols can be oxidized to produce ketones. The general formula of long chain aliphatic hydroxyketones are C<sub>n</sub>H<sub>2n</sub>O<sub>2</sub>, n = 25 – 65. The hydroxy ketones such as Dihydroxyacetone (Active ingredient in "bronzers" that provide fake suntan coloration; reacts with dead, outer skin cells to produce a dark color; which fades as the dead skin cells slough off) [4]. 2-Heptanone found in oil of clove is also found present in the odor of many fruits and dairy products, and is also responsible for the odor of blue cheese [5]. The compound 36, 47-dihydroxyhenpentacontan-4-one was isolated from essential oil of *Achyranthus asperara* shoot, and showed very high antimicrobial activity as reported by T. N. Mishra et al 1991(structure no 27, table1)[58]. Robin L et al demonstrated physiological interplay between tetracycline (Hydroxy Ketone) and calcium, leading to such effects as altered drug uptake and distribution, decreased bacteriostatic action, tooth staining in newborns of women who have been administered such drug during second or third trimesters of pregnancy as well as in children, also in inhibition of osteogenesis and mineralization in developing bone tissue. The calcium ion apparently provides the most optimal "fit" to phenacyl alcohol chelate ring, as demonstrated by near-ideal bond angles and distances found in solid-state structure of 2:1 complex, but may suffer from some ligand-ligand

steric interactions [6]. Many pharmacologically active drugs, including anti-inflammatories and antitumor agents, bear alpha-hydroxyketone functionality. Alpha hydroxy ketones also act as ion-selective binding agents [6]. Raspberry ketones give a fruity aroma to foods, cosmetics and scents for perfumes, Chie Morimoto et al was described in their study on "Anti-obese action of raspberry ketone" that structure of raspberry ketone is similar to synephrine and capsaicin. Both synephrine and capsaicin are known to have actions that are performed as anti-obese [7]. The study in rats was shown to both prevent, as well as improve, the incidence of fatty liver and obesity. Raspberry ketones have been used for GI maladies, diabetes, fever and relief from painful periods. It is also said to relieve pain of delivery and labor and prevent miscarriages [8]. Ketone bodies (also called ketoacids) may not only treat, but also prevent Alzheimer's disease. Further, this is a potential treatment for Parkinson's disease, Huntington's disease, multiple sclerosis and amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease), drug resistant epilepsy, brittle type I diabetes, and diabetes type II, where there is insulin resistance. Ketone bodies may help the brain to recover after loss of oxygen in newborns though in adults it may help the heart to recover after an acute attack, and may shrink cancerous tumors. Children with drug resistant epilepsy sometimes respond to an extremely low carbohydrate ketogenic diet. MCT oil appears to be useful as an aid in weight loss and body builders use it to improve their lean body mass. Our cells can use ketone bodies as an alternative fuel when glucose is not available [10, 11]. Brain cells, specifically neurons, are very limited, normally they require glucose (sugar), but they can also use ketone bodies. Humans may not normally have ketone bodies circulating and available to the brain unless they have been starving for a couple of days or longer, or consuming ketogenic (very low carbohydrate) diet, such as Atkins. In Alzheimer's disease, neurons in certain areas of the brain are unable to take up glucose [9, 10, 11].

**Biological activity in plants:** Exploration of chemical constituents of plants and their pharmacological screening may provide us the basis for developing leads for development of novel agents. In addition, herbs also provide us some of the very important life saving drugs used in armamentarium of modern medicine. However, among the estimated 250000 – 400000 plant species, only 6% have been studied for their biological activity, and about 15% have been investigated phytochemically [1, 2]. In the present study, we also discuss the Anticancer,

Antimicrobial and Antioxidant activities of plants which is reported in table 2.

**Anticancer activity:** The antitumor activity of medicinal-plant-derived compounds may result from a number of mechanisms, including effects on cytoskeletal proteins that play a key role in cell division, inhibition of DNA topoisomerase enzymes, antiprotease or antioxidant activity, stimulation of the immune system, etc. [12]. The first thing to be understood is that cancer is a multistep process. No one genetic change may cause a cancer; rather several changes must accumulate over time. There are four major classes of genes that are disrupted in cancer formation. Firstly, we have proto-oncogenes, which are normal genes that tend to promote cell division (cell 'growth'). When mutated in a fashion that tends to cause cancer (e.g. becoming unregulated, or autonomous), they are named oncogenes (cancer-causing genes). Usually, cell proliferation is caused by binding of a growth factor to its specific receptor on the cell membrane. This activates the growth factor receptor, which in turn passes the message all the way to the nucleus via several messengers. At the nucleus, instructions required to initiate cell division are read off (transcribed) from the DNA, setting off a chain reaction that ultimately culminates in one cell becoming two. Almost all genes involved in coding for proteins required are potential weakpoints; which if mutated could become oncogenes [13]. For instance, a mutation could cause the cell to display far too many growth factor receptors. Since there is usually excess growth factor floating about, the extra receptors would mean extra signals to the cell to divide and divide. Or perhaps a mutation could transform one of the messengers en route to the nucleus in a way that enhances number of 'division signals' issued per growth factor binding. The second class of genes that, when mutated, can contribute towards cancer formation are the tumour-suppressor genes. Under normal circumstances, this family of genes would apply the 'brakes' to cellular proliferation, limiting the process by keeping it on a short leash. A mutation that disables them would obviously promote neoplasia. An exceptionally common example is the *p53* gene. Staggeringly, over 50% of human tumours contain mutations in this gene. If DNA is damaged, *p53*'s products stop cell's division cycle, and help repair the DNA. If DNA can't be fixed, *p53* orders cell's self-destruction (*apoptosis*), rather than risk cancer. Clearly, knocking out this gene is usually a vital step in the 'strategy' to discover any aspirant cancer [13]. Next up, are the genes regulating apoptosis (programmed cell death). One of the body's most formidable weapons against cancer cells is apoptosis. When a cell becomes

cancerous, the changes can often be recognized by some of the surveillance immune cells. They immediately set about to destroy aberrant cell, often by forcefully initiating its own 'self-destruct' sequence. There are normal genes that promote and inhibit this, and so obviously mutations that wreck this balance in the correct way (inhibit apoptosis' promoters, or promote its inhibitors) will tend to be carcinogenic. Lastly, there are DNA repair genes. The DNA repair gene's loss is an incredible blow to our chances of escaping cancers. It is worth emphasizing again that malignant tumors arise only after a number of mutations have occurred. In fact, "every human cancer that has been analyzed reveals multiple genetic alterations involving activation of several oncogenes and loss of two or more [tumor]-suppressor genes" [13]. In this study many plants having activity against cancer have been reported in table 2. Such as *Annona squamosa* [69,75], *Achyranthes aspera* [81], *Adenocalymma alliaceum* [92], *Artemisia roxburghiana* [103], *Brassica oleracea* [104], *Ichnocarpus frutescens* [150,151], *Prosopis Juliflora* [167], *Petalium murex* [174], but *Wikstroemia chamaedaphne* leaves [179] have been reported for their tumor promoting activity.

**Antimicrobial activity:** Antimicrobial is a substance that kills or inhibits the growth of microorganisms such as bacteria, fungi, or protozoans. Antimicrobial drugs either kill microbes (microbiocidal) or prevent the growth of microbes (micro biostatic) [14]. Most researchers distinguish two groups of antimicrobial agents used in treatment of infectious ailments firstly antibiotics, which are natural substances produced by certain groups of microorganisms, and chemotherapeutic agents, which are chemically synthesized. A hybrid substance is a semisynthetic antibiotic, wherein molecular version produced by microbe is subsequently modified by chemist to achieve desired properties [15]. Mechanisms of action of antibacterial agents have been reported as [16]: 1. Interference with cell wall synthesis: (a.)  $\beta$ -Lactams: penicillins, cephalosporins, carbapenems, Monobactams, (b.) Glycopeptides: vancomycin, teicoplanin. 2. Protein synthesis inhibition: (a.) Binding to 50S ribosomal subunit: macrolides, chloramphenicol, clindamycin, quinupristin-dalfopristin, linezolid, (b.) Binding to 30S ribosomal subunit: aminoglycosides, tetracyclines, (c.) Binding to bacterial isoleucyl- transfer RNA synthetase: mupirocin. 3. Interference with nucleic acid synthesis: (a.) Inhibition of DNA synthesis: fluoroquinolones, (b.) Inhibition of RNA synthesis: rifampin. 4. Inhibition of metabolic pathway: sulfonamides, folic acid analogues, 5. Disruption of bacterial membrane structure: polymyxins, daptomycin. Antibacterial drugs those work by

inhibiting bacterial cell wall synthesis include beta-lactams, such as penicillins, cephalosporins, carbapenems, and monobactams, and glycopeptides, including vancomycin and teicoplanin [17, 18].  $\beta$ -Lactam agents inhibit synthesis of the bacterial cell wall by interfering with the enzymes required for the synthesis of the peptidoglycan layer [18]. Vancomycin and teicoplanin also interfere with cell wall synthesis, but do so by binding to terminal D-alanine residues of the nascent peptidoglycan chain, thereby preventing cross-linking steps required for stable cell wall synthesis [18]. Macrolides, aminoglycosides, tetracyclines, chloramphenicol, streptogramins, and oxazolidinones produce antibacterial effects by inhibiting protein synthesis [17, 18]. Further, some antimicrobial compounds, originally found as products of microorganisms, can be synthesized entirely by chemical means. 14-Keto-16-hydroxynonacosane (structure no. 1) have been isolated from *Brassica oleracea* leaves whereas 16-hydroxy-26-methylheptacosan-2-one was isolated from essential oil of *Achyranthus aspera* shoot, Heptatriacontan-4-one is isolated from *Pedaliium murex* fruits and 5-hydroxyhexacosan-9-one, isolated from *Crinum augustum* bulb are reported in table 1, have showed high antimicrobial activity (table 1 & 2.)

**Antioxidant activity:** Antioxidant is a molecule capable of inhibiting oxidation of other molecules. Oxidation is a chemical reaction that transfers electrons or hydrogen from a substance to an oxidizing agent. Oxidation reactions can produce free radicals which can start chain reactions. When chain reaction occurs in a cell, it can cause damage or death to the cell. Antioxidants terminate these chain reactions by removing free radical intermediates, and inhibit other oxidation reactions. They do this by being oxidized themselves, so antioxidants are often reducing agents such as thiols, ascorbic acid, or polyphenols [19]. The free radical theory of aging, however, has gained strong support because it is able to explain some of the processes that occur with aging and the degenerative diseases of aging. This theory proposes that an increase in oxygen radical production with age by mitochondria produce an increase in cellular damage [20-23]. Indeed, researchers have shown that oxygen utilization by mitochondria of aerobic organisms can generate several reactive radicals, such as superoxide ( $O_2^{\cdot -}$ ), hydrogen peroxide ( $H_2O_2$ ), and possibly hydroxyl radical ( $HO^{\cdot}$ ) [24-26]. In addition, nitric oxide ( $NO^{\cdot}$ ) is also produced by mitochondria [27] and may have implications for the aging process and several disease states associated with aging. Phagocytes are another potent source of oxidant production, and they produce  $O_2^{\cdot -}$ ,  $H_2O_2$ ,  $HO^{\cdot}$ ,  $NO^{\cdot}$

, and hypochlorous acid ( $HOCl$ ) [26, 28-29].  $HOCl$  is an inflammatory mediator and a strongly oxidizing and chlorinating compound that can form other reactive metabolites, such as nitryl chloride ( $NO_2Cl$ ) and nitrogen dioxide ( $NO_2^{\cdot}$ ), in the presence of nitrite [30]. Recently, scientists have shown that activated human polymorphonuclear neutrophils convert nitrite into  $NO_2Cl$  and  $NO_2^{\cdot}$  metabolites, which can significantly contribute to the formation of potentially harmful compounds [31]. The potentially deleterious effects of reactive oxygen, reactive nitrogen, and chlorinating species for simplicity, referred to as oxidants or radicals can affect the aging process. Aerobic organisms are well-protected against oxidative challenges by sophisticated antioxidant defense systems. However, it appears that during the aging process an imbalance between oxidants and antioxidants balance may occur, referred to as oxidative stress. Oxidative stress induced by oxidant species occurs under conditions when antioxidant defenses are depleted or when the rate constants of the radical reactions are greater than the antioxidant defense mechanisms [32]. In subjects with Parkinson's disease, protein carbonyls have been assessed in postmortem of brain tissues and age-matched controls. In brain areas associated with Parkinson's, such as the substantianigra, caudate nucleus, and the putamen, there was a significant increase in protein-bound carbonyl levels [33]. Other markers of protein oxidation are also affected with amyotrophic lateral sclerosis. Researchers investigated amyotrophic lateral sclerosis and found elevated levels of free 3-nitrotyrosine [34]. In summary, these results suggest that levels of oxidized proteins increase with age and results in several neurodegenerative aging-associated diseases. Metal-catalyzed oxidation reactions could be partly responsible for protein oxidation; however, there are multitudes of other oxidative reactions, which can generate protein carbonyls and other oxidative modifications in proteins and amino acids. Reactive nitrogen species could nitrate proteins and have major physiological consequences on normal protein function. Thus, reactive metabolites from oxygen and nitrogen metabolism could be active players in aging and the degenerative diseases of aging. Parkinson's disease involves loss of dopaminergic neurons, especially in the midbrain area called substantianigra. Oxidative stress is known to play a major role in destruction of these neurons. For example, since  $Fe^{+3}$  is increased in substantianigra [35] and hydrogen peroxide is also produced during dopamine metabolism in the dopaminergic neurons [36], there is possibility of  $Fe^{+3}$  catalyzed production of hydroxyl radicals which will result in significant damage to these neurons. Hydroxyl radical production also increased when

mitochondrial respiratory chain dysfunctions, has been found in diverse tissues of Parkinson's patients [37]. *Annona squamosa* [76], *Achyranthes aspera* [82], *Brassica oleracea* [106,105], *Cassia auriculata* [115], *Curculigo orchioides* [137], *Hyoscyamus muticus* [146], *Ichnocarpus frutescens* [147], *Neolitsea serica* [153], *Prosopis Juliflora* [168], *Pedaliium murex* [174,178] showed very high antioxidant activity as reported in the table 2.

## CONCLUSION

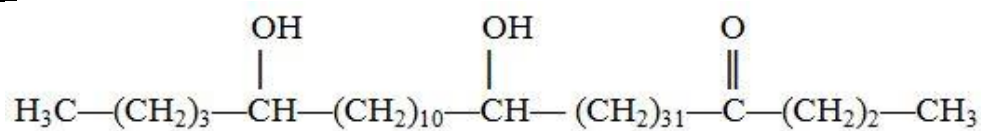
Plant products represent an outstanding source of compounds which are able to play an important role in the treatment of several human diseases. As

important drug development references from natural products, attempts have been made for inventions of new aliphatic hydroxy ketones from medicinal plants alongwith exploring their possible modes of action in our journey to fight against cancer and neuro-generative diseases.

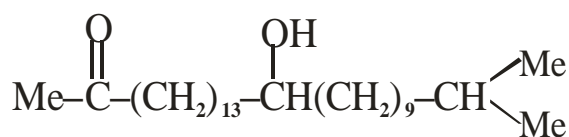
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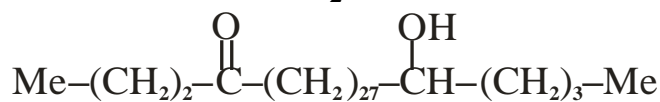
## Structures



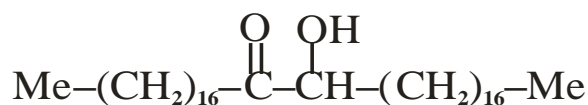
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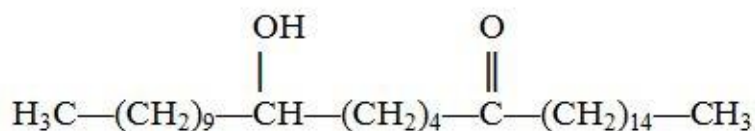
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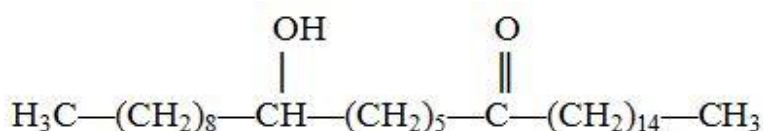
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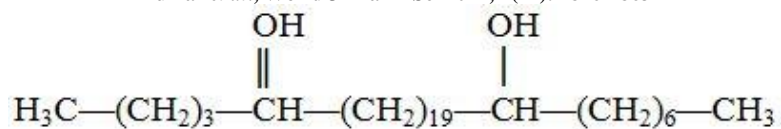
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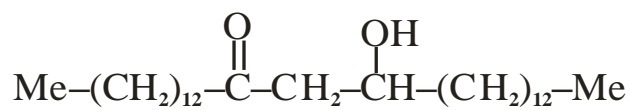
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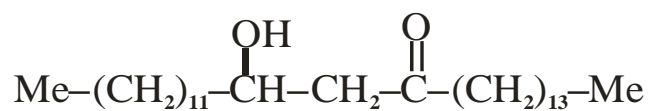
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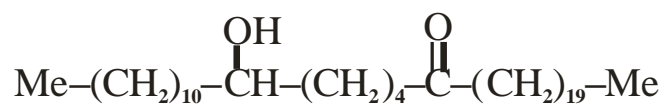
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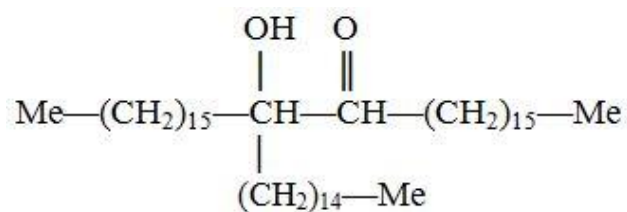
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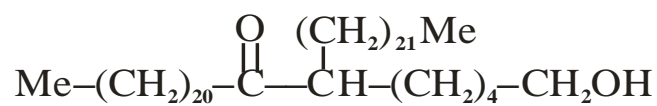
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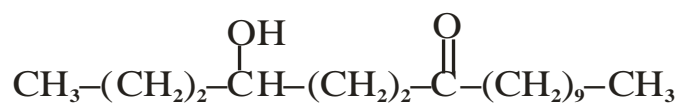
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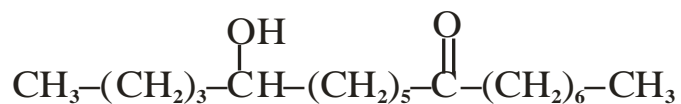
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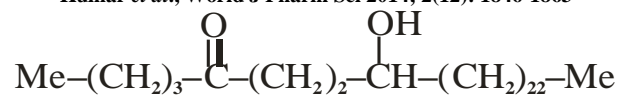
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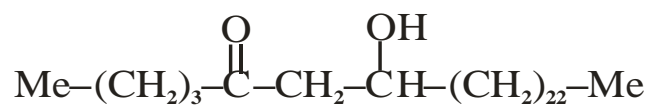
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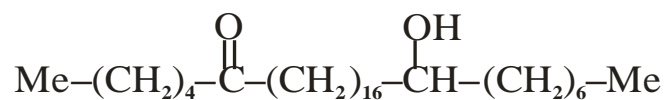
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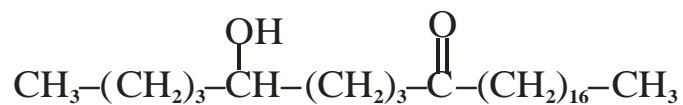
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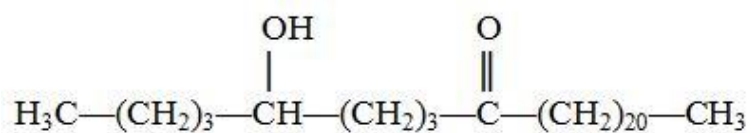
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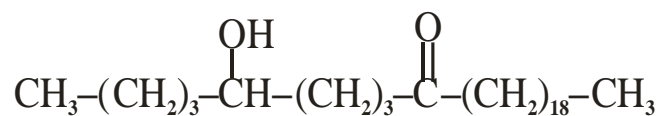
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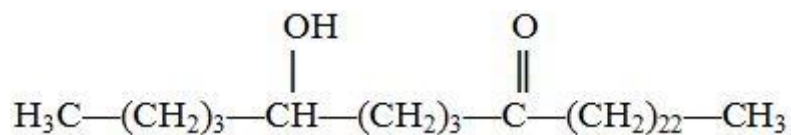
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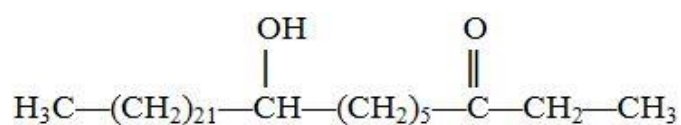
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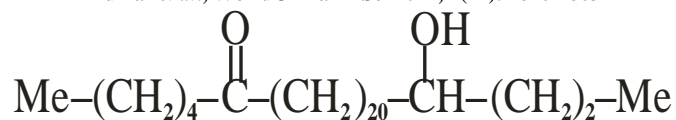
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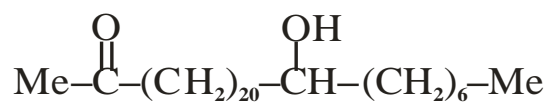
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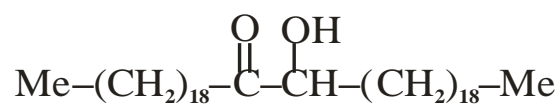
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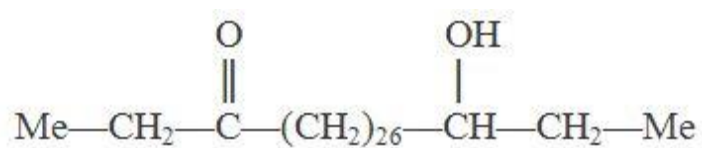
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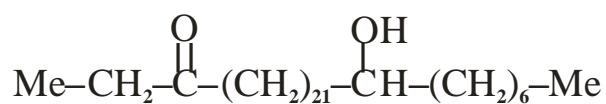
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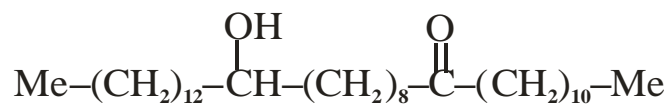
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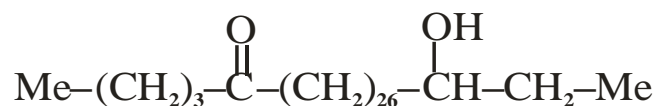
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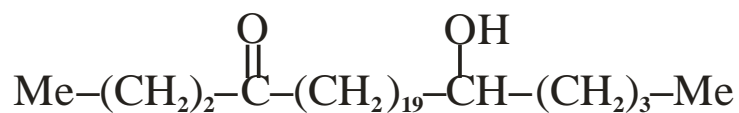
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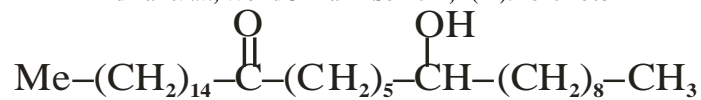


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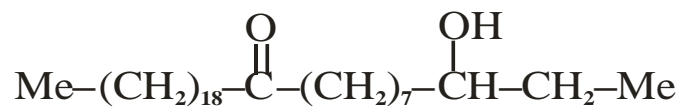


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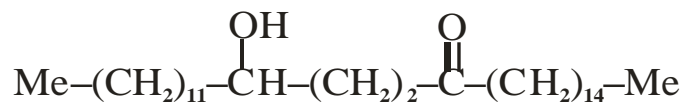




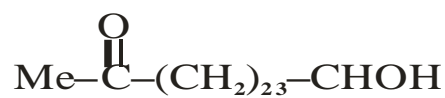
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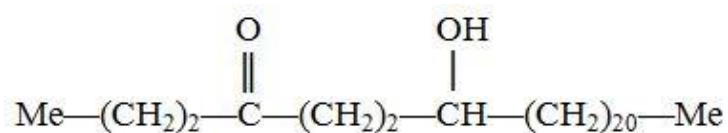
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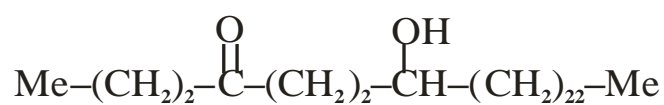
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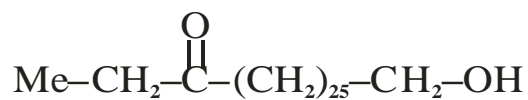
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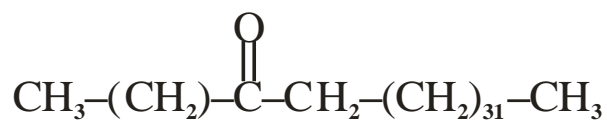
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**Table 1. Review of Thirty eight long chain aliphatic hydroxy ketones isolated from different plant material and their molecular formula with melting points.**

Entry	Plant names	Part Used	Compounds	M.P. (°C)	MF	Structure no.	Ref.
1.	<i>Achyranthes aspera</i>	Shoot	36, 47-dihydroxyhenpentacontan-4-one	78-79	C <sub>51</sub> H <sub>102</sub> O <sub>3</sub>	1	58
			16-hydroxy-26-methylheptacosan-2-one	71-72	C <sub>28</sub> H <sub>56</sub> O <sub>2</sub>	2	60
2.	<i>Adenocalymma alliaceum</i>	Leaves	32-Hydroxyhexatriacontan-4-one	75-76	C <sub>36</sub> H <sub>72</sub> O <sub>2</sub>	3	56
			19-Hydroxyhexatriacontan-18-one	82-83	C <sub>36</sub> H <sub>72</sub> O <sub>2</sub>	4	56
3.	<i>Annona squamosa</i>	Leaf cuticular waxes	11-hydroxy-16-hentriacontanone	-	C <sub>31</sub> H <sub>62</sub> O <sub>2</sub>	5	67
			10-hydroxy-16-hentriacontanone	-	C <sub>31</sub> H <sub>62</sub> O <sub>2</sub>	6	67
4.	<i>Artemisia roxburghiana</i>	shoot	8-Hydroxydotriacontan-28-one	-	C <sub>32</sub> H <sub>64</sub> O <sub>2</sub>	7	50
5.	<i>Brassica oleracea</i>	Leaves	14-Keto-16-hydroxynonacosane	-	C <sub>29</sub> H <sub>58</sub> O <sub>2</sub>	8	38
			15-Keto-13-hydroxynonacosane	-	C <sub>29</sub> H <sub>58</sub> O <sub>2</sub>	9	38
6.	<i>Cassia auriculata</i>	Leaves	26-Hydroxyheptatriacontan-21-one	83-84	C <sub>37</sub> H <sub>74</sub> O <sub>2</sub>	10	39
			18-Hydroxy-18-pentadecyltetracontan-17-one	80	C <sub>49</sub> H <sub>98</sub> O <sub>2</sub>	11	39
			6-Doacosan-1-hydroxyoctacosan-7-one	88	C <sub>50</sub> H <sub>100</sub> O <sub>2</sub>	12	39
7.	<i>Chiococca alba</i>	Leaves	4-hydroxyheptadecan-7-one	-	C <sub>17</sub> H <sub>34</sub> O <sub>2</sub>	13	66
			5-hydroxyoctadecan-11-one	-	C <sub>18</sub> H <sub>36</sub> O <sub>2</sub>	14	66
8.	<i>Costus speciosus</i>	Roots	24-hydroxyhentriacontan-27-one	84-85	C <sub>31</sub> H <sub>62</sub> O <sub>2</sub>	15	46
			24-Hydroxytriacontan-26-one	81	C <sub>30</sub> H <sub>60</sub> O <sub>2</sub>	16	46
			8-Hydroxytriacontan-25-one	95	C <sub>30</sub> H <sub>60</sub> O <sub>2</sub>	17	47
9.	<i>Crinum augustum</i>	Bulbs	5-hydroxyhexacosan-9-one	-	C <sub>26</sub> H <sub>52</sub> O <sub>2</sub>	18	64
			5-hydroxytriacontane-9-one	-	C <sub>30</sub> H <sub>60</sub> O <sub>2</sub>	19	64
			5-hydroxyoctacosan-9-one	-	C <sub>28</sub> H <sub>56</sub> O <sub>2</sub>	20	64
			5-hydroxydotriacontan-9-one	-	C <sub>32</sub> H <sub>64</sub> O <sub>2</sub>	21	65
			23-hydroxyhentriacontan-29-one	-	C <sub>31</sub> H <sub>62</sub> O <sub>2</sub>	22	65
10.	<i>Curculigo orchioides</i>	Rhizomes	27-Hydroxytriacontan-6-one	84-85	C <sub>30</sub> H <sub>60</sub> O <sub>2</sub>	23	53
			23-Hydroxytriacontan-2-one	109-110	C <sub>30</sub> H <sub>60</sub> O <sub>2</sub>	24	53
			21-Hydroxytetracontan-20-one	77-79	C <sub>40</sub> H <sub>80</sub> O <sub>2</sub>	25	54
11.	<i>Duboisia myoporoides</i>	Leaves	3-Hydroxydotriacontan-30-one	75-76	C <sub>32</sub> H <sub>64</sub> O <sub>2</sub>	26	51
			8-Hydroxydotriacontan-30-one	76-77	C <sub>32</sub> H <sub>64</sub> O <sub>2</sub>	27	52
12.	<i>Grewia populifolia</i>	Leaves	Tetracontan-21-ol-12-one	82-83	C <sub>34</sub> H <sub>68</sub> O <sub>2</sub>	28	45
13.	<i>Hyoscyamus muticus</i>	Leaves	3-Hydroxytetracontan-30-one	76-77	C <sub>34</sub> H <sub>68</sub> O <sub>2</sub>	29	44

14.	<i>Ichnocarpus frutescens</i>	Whole plant	5-Hydroxyoctacosan-25-one	-	C <sub>28</sub> H <sub>56</sub> O <sub>2</sub>	30	55
15.	<i>Machilus gleucescens</i>	Leaves	n-Hentriacontan-10-ol-16-one	96	C <sub>31</sub> H <sub>62</sub> O <sub>2</sub>	31	49
16.	<i>Marsilea minuta</i>	Leaves	3-Hydroxytriacontan-11-one	102-103	C <sub>30</sub> H <sub>60</sub> O <sub>2</sub>	32	40,41
17.	<i>Neolitsea serica</i>	Leaves	13-Hydroxyhentriacontan-16-one	83	C <sub>31</sub> H <sub>62</sub> O <sub>2</sub>	33	42
18.	<i>Pedaliium murex</i>	Fruit	Heptatriacontan-4-one	-	C <sub>36</sub> H <sub>72</sub> O	38	63
19.	<i>Prosopis Juliflora</i>	Bark	Hexacosan-25-one-1-ol	65	C <sub>26</sub> H <sub>52</sub> O <sub>2</sub>	34	43
20.	<i>Tanacetum nubigenus</i>	Leaves	22-Hydroxyoctacosan-25-one	70-71	C <sub>28</sub> H <sub>56</sub> O <sub>2</sub>	35	57
			24-Hydroxytriacontan-27-one	73-74	C <sub>30</sub> H <sub>60</sub> O <sub>2</sub>	36	57
21.	<i>Wikstroemia chamaedaphne</i>	Leaves	29-Hydroxynonacosan-3-one	-	C <sub>29</sub> H <sub>58</sub> O <sub>2</sub>	37	48

**Table 2. Record of Plant species and their medicinal value with biological activities, from where long chain aliphatic hydroxyl ketones were isolated**

Entry	Plant names	Part used	Medicinal /Traditional uses	Biological activities
01	<i>Achyranthes aspera</i> (Linn.) ( <i>Amaranthaceae</i> )	Whole plant, seed, root,	Against cough, bronchitis, rheumatism, malarial fever, dysentery, asthma, renal and cardiac dropsy, hypertension and diabetes mellitus [76]. Stimulate the immunity, enhance the antigen clearance, potentiate antibody production, and elevate thyroid hormone levels [77].	Antiperiodic, Antiphlegmatic Spermicidal, Anti-allergic Nephroprotective, Antiparasitic, Hypoglycemic, Analgesic, Antipyretic [76,80], Antiviral Anticarcinogenic [81], Antioxidant [82], Chemopreventive, Anti-inflammatory, Anti-arthritis [77,79].
02	<i>Adenocalymma alliaceum</i> (Lam.) Miers. ( <i>Bignoniaceae</i> )	Garlic creeper leaves, root, flower	Astringent[83], treat against colds, fevers and headaches [85,86,87], remedy for the pain and inflammation of arthritis and rheumatism, flu, fever, act as a whole body tonic [81], lowered serum cholesterol levels [90, 91] depurative, purgative, and vermifuge [92].	Antimicrobial [83,89], Antifungal, Antiaflatoxicogenic [84], Antimycotic, Analgesic, Antiarthritic, Anti-inflammatory [88], Antipyretic Antirheumatic, Antitussive, Anticancer activity [92].
03	<i>Annona squamosa</i> (Linn.)	Fruits, seed, juices, young leaves, root,	Hair tonic, to kill the head and body lice (70), diabetes (70), epilepsy, dysentery, cardiac problems, worm	, Antitumoral [68,69], Antilarvicidal [70], Insecticidal [71], Antidiabetic [72],

	( <i>Annonaceae</i> )	bark.	infestation (71), constipation, haemorrhage, dysuria, fever, and ulcer.	Antimicrobial [73], Anticancerous [74,75], Antioxidant [76].
04	<i>Artemisia roxburghiana</i> (Bess.) ( <i>Asteraceae</i> )	Leaves, stem	Effective against parasites including Leishmania [95], Schistosoma [96], Toxoplasma [97] and Trypanomosa [98]. hepatitis B [99], breast cancer, human leukaemia, colon, small-cell lung carcinomas [101], tonic, skin allergy [102], cooling purposes (Leaves), against malaria (Plant decoction), and intestinal worms. [103].	Antiviral activities [99,100], Anticancer, Antimalarial [93], Antiseptic and Anti inflammatory [103].
05	<i>Brassica oleracea</i> (var.) capitata. ( <i>Winnigstadt</i> )	Flower (Inflorescences), leaves	Tonic, acute inflammation,[107].	Broad antibiotic properties – including nematocidal, Antiprotozoal, Insecticidal, Anticancer, Antitumor, Lipid peroxidation and Augmenting, transaminase [104], Antioxidant and Antimicrobial [106,105].
06	<i>Cassia auriculata</i> L. ( <i>Fabaceae</i> )	Flowers, leaves, bark, fruits, seeds, root	Diabetes, mellitus [109,110], rheumatism, conjunctivitis and diabetes [111], ‘Avarai Panchaga Choornam’ the main constituent of Kalpa herbal tea [108], astringent, leaves and fruits anthelmintic, eye troubles and skin diseases [116], ulcers, leprosy and liver disease [113].	Antidiabetic, Antiperoxidative [119], Antibacterial, Hepatoprotective [114], Antipyretic [118], Antidiabetic, Hypolipidemic[117], and Antioxidant[115].
07	<i>Chiococca alba</i> L. (Hitch.) ( <i>Rubiaceae</i> )	root	Against snake bite [119], laxative, diuretic, emetic.	DNA-interacting activity[121], Antifungal [122], and Antidiarrhoeal [120].
08	<i>Costus speciosus</i> (Koen.) SM. ( <i>Zingiberaceae</i> )	rhizomes, leaves, roots, Juice (rhizome), stem	Constipation, skin diseases, fever, asthma, bronchitis, inflammation, anemia, astringent, purgative, aphrodisiac [123,133], smooth muscle relaxant action, diuretic, cardio tonic, central nervous system depressant [123], rheumatism, diabetes [127, 128, 129], astringent [127, 128 129, 130, 131], acrid, cooling, aphrodisiac [125,128,131], purgative [127-130], anthelmintic [128,127,129,130,131], depurative [125,127,130,131] febrifuge, expectorant, tonic [125,127], improves digestion [128] stimulant	Anticholinesterase [123], Antifungal [124], Anti-inflammatory, Antipyretic [123], Antiarthritic [123], CNS depressant [130,132], Hepatoprotective [125], Antivermin [130], and Antispasmodic [132].

			[128,127,132], clears toxins, headache [127], pneumonia, dropsy, urinary diseases, jaundice, mental disorders, dysentery [125], sudorific, leprosy, for abortion [125].	
09	<i>Crinum augustum</i> (Rox.) (Amaryllidaceae)	bulbs	Alzheimer's disease, against foul, [134]	Biofouling activity [134], Antifungal, cytotoxic, Analgesic, Anti-inflammatory and Antimicrobial [135].
10	<i>Curculigo orchioides</i> (Gaertn.) (Amaryllidaceae)	Root stocks, rhizomes	Tonic, bestorative, aphrodisiac, alterative, demulcent, restorative, depurative, skin diseases [137], attain longevity, memory, youth fullness [139], cooling, diuretic, virilogenic, hemorrhoids, leucorrhoea, pruritis, asthma, bronchitis and jaundice, [140].	Antimicrobial [136], Immunomodulatory, Antioxidant [137], Wound healing [138], Hepatoprotective [140], and Antibacterial [141].
11	<i>Duboisia myoporoides</i> (R. Br.) (Apocynaceae)	Leaves	Motion sickness, stomach disorders, and cancer therapy. [142].	Native antidote against ciguatera poisoning [143].
12	<i>Grewia populifolia</i> (Vahl) (Malvaceae)	Stem bark, root, fruits	Diuretic, spermatorrhoea	Antidiarrhoeal [145], and Anti-inflammatory [144].
13	<i>Hyoscyamus muticus</i> (L.) (Solanaceae)	Root	Relieve pain	Antioxidant [146].
14	<i>Ichnocarpus frutescens</i> (L.) W. T. Aiton. (Apocynaceae)	Leaves, stem and root	Asthma, fever, inflammatory diseases, headache [148], jaundice, diabetes [150], gout, rheumatism, cold [151], blood purifier [152].	Antioxidant [147], Analgesic, Anti-inflammatory [149], Antitumor [150, 151], and Wounds healing [150],
15	<i>Machilus gleucescens</i> (Nees.) Wight. (Lauraceae)	Leaves	Not Reported	Not Reported
16	<i>Marsilea minuta</i> (Linn.) (Marsileaceae)	Whole plant	Insomnia and other mental disorders [154]	Antibacterial [153], Anticonvulsant, Antidepressant [154], Anxiolytic [155].
17	<i>Neolitsea serica</i> (Blume.) (Lauraceae)	Leaves, seed, stems, twigs	Against burning [158], cosmetic products, [159], make candles as well as soaps [160].	Anti-inflammatory [156], Antioxidant, and Anti-aging [159,157].

18	<i>Prosopis Juliflora</i> (Sw.) DC. ( <i>Fabaceae</i> )	Pods, leaves, seeds, bark	Juice is used against cancerous condition terms "superfluous flesh", cathartic, cyanogenetic, discutient, emetic, poison, stomachic, vulnerary, mesquite is a folk remedy for catarrh, colds, diarrhea, dysentery, excrescences, eyes, flu, head cold, hoarseness, inflammation, itch, measles, pinkeye, stomachache, sore throat, wounds, hot tea for sore throat [161,162], treat eye problems, open wounds, dermatological ailments and digestive problems [163,164].	Antiseptic, Antibacterial, Antifungal [165,166]. Antitumor [167], Antioxidant [169], Nitrogen-fixing potential [168,170], Antiemetic [171], and Anti radical [172].
19	<i>Pedaliium murex</i> n (Linn.) ( <i>Pedaliaceae</i> )	Fruit, Stem bark	Reproductive disorders which are mainly impotency in men, nocturnal emissions, gonorrhoea as well as leucorrhoea in women, urinary track disorder as well as gastro intestinal tract disorders [174], and Aphrodisiac,[176]	Suspending agent, [173], Antiulcerogenic, Nephroprotective, Hypolipidemic, Aphrodisiac, Antioxidant, Antimicrobial, Insecticidal [174,178], Antiuro lithiatic [175], Curative effects, fertility enhancing [176], and Antimicrobial [177].
20	<i>Tanacetum nubigenum</i> (Wallich ex. DC.) ( <i>Compositae</i> )	Aerial parts, Whole plant Leaf, Fruit	Herbal Perfume[57], as incenses [182], energy Syrup[185]	Antimicrobial [183, 184]
21	<i>Wikstroemia chamaedaphne</i> (Bunge) Meisn. ( <i>Thymelaeaceae</i> )	leaves	the treatment of hepatitis[181]	Acaricidal [179], and Tumor promoting effects [180].

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