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Cannabis Sativa: Therapeutic Chemistry and Classification

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Review Article

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ABSTRACT

Cannabis sativa is an herbaceous plant in the Cannabis class types of Cannabaceae family. It's utilized as a wellspring of mechanical fiber, seed oil, sustenance, entertainment, religious and otherworldly dispositions, and medication. The expression "cannabinoids" speaks to a gathering of C_{21} terpenophenolic mixes found up to this point interestingly in *Cannabis sativa* L. As a result of the improvement of engineered cannabinoids (e.g., nabilone, HU-211 (dexanabinol or ajulemic corrosive) and the disclosure of the artificially unique endogenous cannabinoid receptor ligands ("endocannabinoids," e.g., anandamide, 2-arachidonoylglycerol), the expression "phytocannabinoids" was proposed for these specific Cannabis constituents. The primary psychoactive constituent of Cannabis is tetrahydrocannabinol (THC); the plant is known to contain more than 500 mixes, among them no less than 113 cannabinoids. In conventional solution of India specifically C. sativa has been utilized as psychedelic, entrancing, soothing, pain relieving, and against inflammatory agent.

INTRODUCTION

With a stock of a few hundreds auxiliary metabolites distinguished, *Cannabis sativa* L. (hemp) is one of the phytochemical best described plant species. The biomedical significance of hemp without a doubt underlies the abundance of information on its constituents and their natural exercises, and cannabinoids, a class of novel meroterpenoids got from the alkylation of an olive to alkyl resorcinol with a monoterpene unit, are the most run of the mill constituents of Cannabis [1-4]. Notwithstanding the outstanding psychotropic properties of Δ9-THC, cannabinoids have been accounted for to show potential in different fields of solution, with the ability to address neglected necessities like the help of chemotherapy-inferred queasiness and anorexia, and symptomatic alleviation of numerous sclerosis [5-12]. A considerable lot of the potential restorative employments of cannabinoids are identified with the cooperation with (no less than) two cannabinoid G-protein coupled receptors (CB1 and CB2). Be that as it may, various exercises, similar to the antibacterial or the antitumor properties are non-absolutely needy or completely autonomous from the cooperation with these proteins [13-18]. These pharmacological exercises are especially intriguing since, on a basic level, they could be effortlessly separated by the undesirable psychotropic impacts.

Cultivars

Cultivars basically developed for their fiber, described by long stems and small fanning. Cultivars developed for seed which can be eaten totally crude or from which hemp oil is separated. Cultivars developed for restorative or recreational purposes. An ostensible if not legitimate qualification is regularly made between mechanical hemp, with convergences of psychoactive mixes awfully low to be valuable for that reason, and marijuana [19-23].

CHEMISTRY AND CLASSIFICATION

The significant dynamic rule in all cannabis items is Δ9-tetrahydrocannabinol (Δ9-THC or just THC), additionally known by its International Non-Proprietary Name (INN) as dronabinol. The unsaturated security in the cyclohexene ring is situated between C-9 and C-10 in the more regular dibenzopyran ring numbering framework. There are four stereoisomers of THC, however just the (−) - Trans isomer happens actually (CAS-1972-08-03)[24-27]. The completely orderly name for this THC isomer is (−)- (6aR,10aR)- 6,6,9-trimethyl-3-pentyl-6a,7,8,10a-tetrahydro-6H-benzo[c]chromen-1-ol. Two related substances, Δ9-tetrahydrocannabinol-2-oic corrosive and Δ9-tetrahydrocannabinol-4-oic corrosive (THCA), are additionally present in cannabis, now and then in substantial

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sums. Amid smoking, THCA is halfway changed over to THC. The dynamic isomer Δ8-THC, in which the unsaturated security in the cyclohexene ring is situated between C-8 and C-9, is found in much littler sums [28-32].

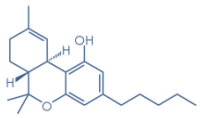

Figure 1: Molecular formula: $C_{21}H_{30}O_2$, Molecular weight: 314.4 g/mol

In this way, 66 cannabinoids have been recognized. They are separated into 10 subclasses.

1. Cannabigerol (CBG) sort: CBG was the main cannabinoid distinguished and its antecedent cannabigerolic corrosive (CBGA) was appeared to be the principal biogenic cannabinoid shaped in the plant. Propyl side-chain analogs and monomethyl ether subordinate are different cannabinoids of this gathering.

2. Cannabichromene (CBC) sort: Five CBC-sort cannabinoids, principally present as C5-analogs, have been recognized.

3. Cannabidiol (CBD) sort: CBD was disengaged in 1940; however its right structure was initially explained in 1963 by Mechoulam and Shvo. Seven CBD-sort cannabinoids with C1 to C5 side chains have been portrayed. CBD and its comparing corrosive CBDA are the richest cannabinoids in fiber-sort Cannabis (mechanical hemp). Secluded in 1955, CBDA was the initially found cannabinoid corrosive.

4. Tetrahydrocannabinol (THC) sort: Nine THC-sort cannabinoids with C1 to C5 side chains are known. The major biogenic antecedent is the THC corrosive A, though THC corrosive B is available to a much lesser degree. THC is the primary psychotropic guideline; the acids are not psychoactive. THC (6a,10a-trans-6a,7,8,10a-tetrahydro-6,6,9-trimethyl-3-pentyl-6H-dibenzo[b,d]pyran-1-ol) was initially disconnected in 1942, yet the right structure task by Gaoni and Mechoulam occurred in 1964.

5. THC sort: THC and its corrosive forerunner are considered as THC and THC corrosive curios, individually. The 8, 9 twofold bond position is thermodynamically more steady than the 9, 10 position - THC is approx. 20% less dynamic than THC.

6. Cannabicyclol (CBL) sort: Three cannabinoids described by a five-particle ring and C1-connect rather than the regular ring A are known: CBL, its corrosive forerunner, and the C3 side-chain simple. CBL is known to be warmth created ancient rarity from CBC. Cannabielsoin (CBE) sort: Among the five CBE-sort cannabinoids, which are ancient rarities shaped from CBD, are CBE and its corrosive antecedents A and B.

8. Cannabinol (CBN) and Cannabinodiol (CBND) sorts: Six CBN-and two CBND-sort cannabinoids are known. With ring A aromatized, they are oxidation curios of THC and CBD, individually. Their fixation in Cannabis items relies on upon age and capacity conditions. CBN was initially named in 1896 by Wood et al. and its structure illustrated in 1940.

9. Cannabitriol (CBT) sort: Nine CBT-sort cannabinoids have been recognized, which are portrayed by extra OH substitution. CBT itself exists as both isomers and the racemate, though two isomers (9-a and 9-b-hydroxy) of CBTV were distinguished. CBDA tetrahydrocannabitriol (ester at 9-hydroxy gathering) is the main reported ester of any normally happening cannabinoids.

10. Random sorts: Eleven cannabinoids of different uncommon structure, e.g., with a furano ring (dehydrocannabifuran, cannabifuran), carbonyl capacity (cannabichromanon, 10-oxo-G-6a-tetrahydrocannabinol), or tetrahydroxy substitution (cannabiripsol), are known.

PHARMACOLOGY

The pharmacology of cannabis is confounded by the nearness of an extensive variety of cannabinoids. At little measurements, cannabis produces rapture, help of nervousness, sedation and sluggishness. In a few regards, the impacts are like those brought about by liquor [33-36]. Anandamide has been distinguished as the endogenous ligand for the cannabinoid receptor and has pharmacological properties like those of THC. At the point when

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cannabis is smoked, THC can be distinguished in plasma close to inward breath; it has a half-existence of 2 hours. Taking after smoking of what might as well be called 10–15 mg over a time of 5–7 minutes, crest plasma levels of Δ9-THC are around 100 μg/L. It is profoundly lipophilic and broadly disseminated in the body. Two dynamic metabolites are shaped: 11-hydroxy-Δ9-THC and 8β-hydroxy-Δ9-THC [37-39]. The first is further metabolized to Δ9-THC-11-oic corrosive. Two dormant substances are likewise shaped — 8α-hydroxy-Δ9-THC and 8α, 11-dihydroxy-Δ9-THC — and numerous other minor metabolites, a large portion of which show up in the pee and defecation as glucuronide conjugates. A few metabolites can be recognized in the pee for up to 2 weeks taking after smoking or ingestion. There is little confirmation for harm to organ frameworks among direct clients; however utilization with tobacco conveys the greater part of the dangers of that substance. Most enthusiasm for the unfavorable properties of cannabis has focused on its relationship with schizophrenia, despite the fact that it is still indistinct if there is a causative connection between psychological wellness and cannabis. Fatalities straightforwardly owing to cannabis are uncommon [40-43].

ESTIMATION OF THE AGE OF CANNABIS SAMPLES

CBN does not exist in crisply and painstakingly dried marihuana. In the event that it is available, the example is comprehended to have begun to corrupt and ought not to be utilized for similar purposes. It is doable to gauge the age of a given marijuana test on the premise of its THC and CBN content, expecting capacity was completed at room temperature. It is therefore that examination for near objects is for the most part not done over three months after example seizure [44-47]. THC seems to corrupt at a higher rate for the main year than for resulting years. One study recommends that examples with a proportion of CBN to THC of under 0.013 are under six months old, and those with a proportion somewhere around 0.04 and 0.08 are somewhere around one and two years of age. However varieties from exploratory conditions ought to be considered when utilizing this way to deal with gauge the time of cannabis tests [48-51].

NONCANNABINOID-TYPE CONSTITUENTS

Terpenoids

The typical aroma of Cannabis results from around 140 various terpenoids. Isoprene units (C5H8) shape monoterpenoids (C10 skeleton), sesquiterpenoids (C15), diterpenoids (C20), and triterpenoids (C30). Terpenoids may be non-cyclic, monocyclic, or polycyclic hydrocarbons with substitution outlines including alcohols, ethers, aldehydes, ketones, and esters. The urgent oil (erratic oil) can without quite a bit of extend be procured by steam refining or vaporization. The yield depends on upon the Cannabis sort (pharmaceutical, fiber) and preparation, sex, age, and part of the plant, advancement (indoor, outdoors), assemble time and conditions, drying and limit. For example, new buds from an Afghani variety yielded 0.29% key oil. Drying and limit decreased the substance from 0.29 after 1 week and 3 months to 0.20 and 0.13%, independently [52-55]. Monoterpenes showed a basically more vital mishap than sesquiterpenes, yet none of the huge fragments completely vanished in the drying strategy. Around 1.3 L of indispensable oil per ton occurred in light of recently gathered outdoors created Cannabis, contrasting with around 10 L/ha. The yield of nonpollinated ("sinsemilla") Cannabis at 18 L/ha was more than twofold differentiated and pollinated Cannabis (8 L/ha). Sixty-eight fragments were recognized by GC and GC/mass spectrometry (MS) in new bud oil refined from high-control, indoor-created Cannabis. The 57 recognized constituents were 92% monoterpenes, 7% sesquiterpenes, and approx 1% distinctive blends [56-58]. The decision monoterpenes were myrcene (67%) and limonene (16%). In the key oil from outdoors created Cannabis, the monoterpene center changed some place around 47.9 and 92.1% of the total terpenoid content. The sesquiterpenes kept running from 5.2 to 48.6%. The most overflowing monoterpene was E-myrcene, trailed by trans-caryophyllene, D-pinene, trans-ocimene, and D-terpinolene. "Cure sort" Cannabis generally contained less caryophyllene oxide than "fiber-sort" Cannabis. For sure, even in "pharmaceutical sort" Cannabis, the THC substance of the key oil was not more than 0.08%. In the key oil of five differing European Cannabis cultivars, the mind-boggling terpenes were myrcene (21.1–35.0%), D-pinene (7.2–14.6%), D-terpinolene (7.0–16.6%), transcaryophyllene (12.2.–18.9%), and D-humulene (6.1–8.7%) [59-62]. The standard complexities between the cultivars were found in the substance of D-terpinolene and D-pinene. Diverse terpenoids show just in takes after are sabinene, D-terpinene, 1,8-cineole (eucalyptol), pulegone, J-terpinene, terpineol-4-ol, bornyl acidic corrosive induction, D-copaene, alloaromadendrene, viridiflorene, E-bisabolene, J-cadinene, trans-E-farnesene, transnerolidol, and E-bisabolol [63- 66].

Hydrocarbons

The 50 known hydrocarbons distinguished in Cannabis comprise of n-alkanes running from C_9 to C_{39}, 2-methyl-, 3-methyl-, and some dimethyl alkanes. The significant alkane show in a fundamental oil got by extraction and steam refining was the n-C_{29} alkane nonacosane (55.8 and 10.7%, individually). Other plenteous alkanes were heptacosane, 2, 6-dimethyltetradecane, pentacosane, hexacosane, and hentriacontane [67-69].

Nitrogen-Containing Compounds

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Cannabis sativa L. is one of the uncommon psychotropic plants in which the focal sensory system action is not connected to specific alkaloids. Be that as it may, two spermidine-sort alkaloids have been recognized among the more than 70 nitrogen-containing constituents. Different nitrogenous mixes found are the quartenary bases choline, trigonelline, muscarine, isoleucine betaine, and neurine. Among the 8 amides are, for instance, N-trans-feruloyltyramine, N-p-coumaroyltyramine, and Ntrans-caffeoyltyramine. Five lignanamide subsidiaries have been confined, including cannabisin A, B, C, and D [70-73]. Twelve straightforward amines, including piperidine, hordenine, methylamine, ethylamine, and pyrrolidine, are known. The three proteins distinguished are edestin, zeatin.

Flavonoids

Twenty-three usually happening flavonoids have been recognized in Cannabis, existing principally as C-/O- and O-glycosides of the flavon and flavonol sort aglycones apigenin, luteolin, quercetin, and kaempferol. Orientin, vitexin, luteolin-7-O-glucoside, and apigenin-7-O-glucoside were the significant flavonoid glycosides display in low-THC Cannabis cultivars [74-77]. The cannflavinsn A and B are one of a kind to Cannabis.

Fatty Acids

An aggregate of 33 distinctive unsaturated fats, primarily unsaturated fats, have been recognized in the oil of Cannabis seeds. Linoleic corrosive (53–60% of aggregate unsaturated fats), linolenic corrosive (15–25%), and oleic corrosive (8.5–16%) are most basic. Other unsaturated fats are γ-linolenic corrosive (1–4%), stearidonic corrosive (0.4– 2%), eicosanoic corrosive (<0.5%), cis-vaccenic corrosive, and isolinolenic corrosive. The immersed unsaturated fats are palmitic corrosive (6–9%), stearic corrosive (2–3.5%), arachidic corrosive (1–3%), behenic corrosive (<0.3%), myristic corrosive, lignoceric corrosive, caproic corrosive, heptanoic corrosive, caprylic corrosive, pelargonic corrosive, capric corrosive, lauric corrosive, margaric corrosive, and isoarachidic corrosive. The unsaturated fat range of Cannabis seeds does not altogether shift in oil created from medication (THC) or low-THC (hemp, fiber) sort Cannabis for the THC substance of Cannabis seeds and seed oil [78-80].

PHARMACOLOGICAL CHARACTERISTICS OF CANNABINOIDS AND OTHER CANNABIS CONSTITUENTS

THC is the pharmacologically and toxicologically most important and best contemplated constituent of the Cannabis plant, in charge of the majority of the impacts of normal Cannabis arrangements. (A MEDLINE look covering the period 1993–2003 and utilizing the catchphrases "tetrahydrocannabinol" and "pharmacology" delivered around 1000 references) [81-83]. THC for the most part acts through official to the CB-1 receptor. The characteristic (-) - Trans isomer of THC is 6-to 100-overlay more intense than the (+) - Trans isomer. It is guaranteed that Cannabis as a polypharmaceutical herb may give two favorable circumstances over. Single-fixing manufactured medications:

(1) The restorative impacts of the essential dynamic Cannabis constituents might be synergized by different mixes.

(2) The symptoms of the essential constituents might be moderated by different mixes.

Hence, Cannabis has been portrayed as a "synergistic shotgun," interestingly, for instance, to dronabinol (manufactured THC, Marinol®), a solitary fixing "silver projectile" [84-85]. A late study thought about the subjective impacts of orally directed and smoked THC alone and THC inside Cannabis arrangements (brownies, cigarettes). THC and Cannabis in both application shapes delivered comparable, measurement subordinate subjective impacts, and there were couple of solid contrasts between the THC-just and whole plant conditions.

ANALYSIS OF PHYTOCANNABINOIDS

Instrumental techniques are regularly utilized for the distinguishing proof, order (e.g., fiber sort, sedate sort), and individualization (e.g., source following) of Cannabis plants and items. As a result of the mind boggling science of Cannabis, division methods, for example, GC or fluid chromatography, frequently combined with MS, are essential for the obtaining of the common compound profiles and the touchy, particular, subjective, as well as quantitative (e.g., THC intensity) assurance of Cannabis constituents [86-88]. In any case, particularly to screen purposes and on location field testing, no instrumental systems like thin-layer chromatography (TLC) and shading responses are useful, as well.

Microscopy

Distinguishing a plant sample as *Cannabis sativa* L. is the initial step. The herbal distinguishing proof of plant examples comprises of physical examination of the in place plant morphology and propensity (leaf shape, male and

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female inflorescences, and so forth.) trailed by the microscopical examination of leaves for the nearness of cystolith hairs. The exceptionally bottomless trichomes, which are available on the surface of the fruiting and blossoming highest points of Cannabis, are the most trademark elements to be found in the minuscule examination of Cannabis items (not fluid Cannabis, hashish oil [89-91]. Once in a while minute confirmation is still accessible in smoked Cannabis deposits.

Color Reactions

It must be focused on those positive responses to shading tests are just hypothetical signs of the conceivable nearness of Cannabis items or materials containing Cannabis items. A couple of different materials, regularly safe and uncontrolled by national enactment or global settlements, may respond with comparable hues to the test reagents. It is compulsory for the lab to affirm such results by the utilization of an option system, which ought to be founded on MS. The most well-known shading spot tests incorporate those created by Duquenois and its adjustments [92-96]. An investigation of 270 distinctive plant species and 200 natural mixes has demonstrated that the Duquenois–Levine alteration is most particular. The quick blue B salt test is the most well-known shading response for the perception of TLC examples yet may likewise be utilized as spot test on a channel paper.

Chromatographic Techniques

Thin-layer chromatography

One-and two-dimensional TLC is suited for the obtaining of subjective cannabinoid profiles from plant material. Quick blue salt B or BB are utilized for perception and result as a part of distinctively shaded spot designs. For quantitation, instrumental TLC coupled to densitometry is vital. High-weight TLC and over pressured layer chromatography have been created for the reproducible and quick assurance and disconnection of unbiased and acidic cannabinoids

Gas chromatography/Mass spectrometry

GC with fire ionization or MS recognition is presently the best settled technique for the investigation of Cannabis and its items [97-98]. Derivatization is fundamental (e.g., silylation or methylation) when data about cannabinoid acids, the ruling cannabinoids in the plant, is required. The aggregate cannabinoid content, i.e., the measure of nonpartisan cannabinoids in addition to the unbiased cannabinoids framed by decarboxylation of the acidic cannabinoids, is resolved when the GC investigation is performed without derivatization (89). GC/MS is the technique for decision for making Cannabis profiles and marks (compound fingerprints), an apparatus for crediting the nation of cause, the states of development (indoor, open air), and a so on.

High-performance liquid chromatography

High Performance fluid chromatography makes conceivable the synchronous assurance of impartial and acidic phytocannabinoids without derivatization. Reversed phase segments and ideally dissolvable customized angle frameworks are required for the partition of major and minor cannabinoids and their relating acids, e.g., for chemo typing (CBD-, THC, CBD/THC-sort and so forth.), assessing the age (proportion acidic/unbiased cannabinoids) of Cannabis, contemplating the impact of assembling procedures and capacity conditions, group examination, or direct measurement of THC in fluid home grown arrangements (e.g., Cannabis tea).

CONTROL STATUS

Cannabis and cannabis gum are recorded in Schedules I and IV of the United Nations 1961 Single Convention on Narcotic Drugs. In Article 1, Paragraph 1, of that Convention, cannabis is characterized as: 'the blossoming or fruiting highest points of the cannabis plant (barring the seeds and leaves when not joined by the tops) from which the gum has not been extricated, by whatever name they might be assigned.' Cannabis tar is characterized as: 'The isolated sap, whether unrefined or filtered, acquired from the cannabis plant.' Along with some of its isomers and stereo chemical variations, Δ9-THC is recorded in Schedule I of the United Nations 1971 Convention on Psychotropic Substances.

Prevalence

Among youthful grown-ups (15-to 34-year-olds), lifetime commonness of cannabis utilize shifts extensively between nations, from 1.0% to 45.1%, with a weighted European normal of 32.2%. A year ago utilization of cannabis in this age assembles ranges from 0.4% to 17.5%. It is assessed that 15.4 million (11.7%) youthful Europeans have utilized cannabis amid the most recent year and 6.5% amid the most recent month. Cannabis is the illegal medication destined to be attempted by European school understudies. In the 24 EU Member States and Norway with ESPAD reviews in 2011, lifetime cannabis use among 15-to 16-year-olds went from 5% in Norway to 42% in the Czech Republic [99]. Sexual orientation proportions additionally differed from solidarity to around 2.5 young men to every young lady.

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Mode of Use

Cannabis is normally smoked, regularly blended with tobacco or in a smoking gadget (bong). Since THC has low water dissolvability, ingestion of cannabis prompts to poor retention. The normal "reefer" cigarette contains around 200 mg of home grown cannabis or cannabis pitch.

Medical Use

1. It can be used to treat Glaucoma.
2. It can help control epileptic seizures.
3. It also decreases the symptoms of a severe seizure disorder known as Dravet's Syndrome.
4. THC slows the progression of Alzheimer's disease.
5. The drug eases the pain of Multiple Sclerosis.
6. muscle spasms
7. It lessens side-effects from treating hepatitis C and increases treatment effectiveness.
8. Marijuana treats inflammatory bowel diseases.
9. It relieves arthritis discomfort
10. Chron's diseases
11. Nausea from cancer chemotherapy

Short-term Effects

Transient memory issues , Serious anxiety, including dread that one is being watched or took after (neurosis), Exceptionally odd conduct, seeing, hearing or noticing things that aren't there, not having the capacity to tell creative ability from reality (psychosis), Panic, Hallucinations, Loss of feeling of individual personality, Brought down response time, Expanded heart rate (danger of heart attack), Expanded danger of stroke, Issues with coordination (disabling safe driving or playing sports), Sexual issues (for guys), Up to seven times more prone to contract sexually transmitted contaminations than non-clients (for females)

Long-term Effects

Decrease in IQ (up to 8 focuses if delayed utilize began in adolescent age), Poor school performance and higher shot of dropping out, Impaired thinking and capacity to learn and perform complex assignments, Bring down life fulfillment, Enslavement (around 9% of grown-ups and 17% of individuals who began smoking as high schoolers), Potential development of sedative abuse, Relationship issues, suggest accomplice brutality, Introverted conduct including taking cash or lying, Monetary troubles, Expanded welfare reliance[100]. More prominent odd of being unemployed.

CONCLUSION

For the most recent decade, worry with wellbeing risks inferable from cannabis has been rising. The hearts, lungs, conceptive capacities, and mental capacities of youngsters have been accounted for to be undermined by marijuana, and such dangers are not to be trifled with. Substantial use by anybody or any utilization by developing kids ought to be demoralized. Albeit decisive confirmation is missing of major, long haul general medical issues brought about by marijuana, they are troubling potential outcomes, and both the reports and the from the earlier probability of formative harm to some youthful clients makes weed utilize a reason for outrageous concern. The current confirmation on strategies of halfway forbiddance demonstrates that fractional preclusion has been as compelling in controlling utilization as total restriction and has involved impressively littler social, legitimate, and financial expenses. On adjust, in this manner, we trust that an approach of halfway disallowance is unmistakably desirable over a strategy of finish forbiddance of supply and utilize. However, advance research ought to be led on the biological, behavioral, developmental, and social results of pot use, on the structure and operation of medication markets, and on the relations of different states of accessibility to examples of utilization.

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