



COMPARISON OF ACEBROPHYLLINE VS THEOPHYLLINE ON CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Abstract

Over the past few decades, there has been a positive increase in the use of pharmaceutical treatment for chronic obstructive pulmonary disease (COPD). Methylamines are often used in COPD patients. Theophylline is a well-known bronchodilator and anti-inflammatory medication, and acebrophylline is a relatively recent addition to contemporary respiratory care. Both are used as adjunctive therapy for patients with stable COPD who are receiving long-acting muscarinic antagonists (LAMAs). One of the world's most pressing public health issues at the moment is chronic obstructive pulmonary disease (COPD). Oral medication therapy is utilised as a second- or third-line maintenance treatment for COPD, while inhaled treatments constitute the first-line maintenance treatment. In comparison to inhaled therapy, oral medications exhibit modest bronchodilator and anti-inflammatory properties, albeit at a lesser concentration. A number of benefits of oral medication therapy include its rapid availability, cloudiest pharmacologic methods of action, convenience of administration, lack of complications with correct inhalational drug deposition in lung airways, and cost-effectiveness.

Keywords: Acebrophylline, COPD management, Sustained release theophylline.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a common and treatable lung disease that causes breathing problems and restricted airflow. It's caused by damage to the airways or other parts of the lungs, which can be due to chronic inflammation from prolonged exposure to gases or particles. COPD can also include emphysema and chronic bronchitis. COPD is viewed as an arising general medical condition with an Assessed worldwide predominance of 11.7% [1]. It has been as of now Positioned fourth among driving reasons for mortality around the world in any case, is projected to be the third driving reason in resulting Peasecod has been defined by The Worldwide Drive for Obstructive Lung Sickness. (GOLD) as an infection state portrayed via airflow limit that isn't completely reversible. The ongoing airflow constraint normal for COPD is brought about by a combination of little aviation route infection (obstructive bronchiolitis) and parenchymal obliteration (emphysema), the general commitments of which change from one individual to another [2]. COPD is a main source of bleakness and mortality overall and a significant general medical condition. It is a social and monetary weight in our nation with respect to cost of treatment, loss of man-days. GOLD appraisals propose that COPD will ascend from the 6th to the third most normal reason for death overall by 2020. By and by, COPD is the fourth driving reason for death and influences >16 million individuals in the US (3). Multiple million passing's happened ever year due to COPD representing 6% of all worldwide deaths [4]. The illness Is related with critical dismalness and mortality conveying Significant and growing financial weight worldwide [5]. The weight of COPD is expanding even in emerging nations Like India albeit the greatness of weight of sickness isn't Precisely characterized. The commonness of COPD in India is assessed to be 3.67% with yearly death pace of 500,000 [6].

Chemical and physical properties of Acebrophylline

Acebrophylline is a synthetic compound that Comprises chiefly of Arborol and Theophylline-7Acetic acid derivation. Theophylline-7-Acetic acid derivation content Carboxylic gathering which was fortified with Arborol amino gathering in a stoichiometric proportion of 38.7% corrosive and 61.3% base. In this, Arborol Shows a high plasma organization level Contrasted with Theophylline-7-Acetic acid derivation. Acebrophylline shows a 45% improvement in lung Wellbeing when

contrast and Arborol alone [1].

Acebrophylline is gotten by designated salsify-cation of the Arborol base [trans-4(2- amino-3,5 dibromobenzylamino) cyclohexane] and theophylline 7 acidic corrosive. The carboxyl gathering of theophylline 7 acidic corrosive was salaried with Arborol amine bunch in a stoichiometric proportion (38.7% corrosive and 61.3% base) that guarantees, after absorption, high plasma levels of Arborol with low levels of the xanthine subordinate which are by the by sufficiently high to guarantee a transporter impact for Arborol-old. This impliesthat one hour after administration lung levels of Arborol are 45% higher than in subjects treated with Arborol alone.

- **Mechanism action of Acebrophylline**

Studies have taken a gander at the consolidated activity of the two parts of Acebrophylline on the development of aspiratory surfactant and the advantages Concerning bodily fluid guideline and Microkinetic, what's more, the mitigating autoreactive activity fundamental for clearing bronchial block.

1. **Synthesis and release of pulmonary surfactant**

Surfactant creation in the rodent was analyzed, with regards to levels of all out phospholipids and phosphatidylcholine in BAL following five days' treatment with Acebrophylline, and in an untreated control Bunch. An expansion in the surfactant phospholipid Lattice was obvious only two hours after the last Portion, and the ascent was essentially more noteworthy in the Treated bunch (161±11 mcg/mL) than in controls (139±3.6 mcg/mL) around 18 hours after the last Portion. To evaluate the component by which Acebrophylline invigorates aspiratory surfactant Combination and delivery, the medication's impact was researched on the take-up of marked surfactant forerunners in rodent lung cuts, to perceive how much the Tissue was animated to create surfactant.

The take-up of 14C-choline, one of the forerunners of Phosphatidylcholine was contrasted and that of 32P-phosphate, a phospholipid forerunner, in rodents Treated for five days with Acebrophylline, or its Parts independently: Arborol and theophylline 7 Acidic corrosive. Contrasted with controls 14C-choline take-up in phosphatidylcholine was altogether higher after Acebrophylline and Arborol; theophylline 7 acidic corrosive likewise would in general increment take-up yet not fundamentally. With 32P-phosphate Acebrophylline expanded take-up fundamentally more Than controls, which had a similar impact as Arborol; once more, theophylline-7 acidic corrosive tended to Increment take-up, yet not altogether the way that Acebrophylline actuated the take-up of marked choline as well as of 32Pphosphate proposes it follows up on two levels on surfactant amalgamation: the first includes Arborol lashed activity on phosphocholine-cytidyl-transferase (2). And the second most likely in view of Theophylline-7 acidic corrosive's activity on choline-kinase. In refined kind II pneumocystis from bunny BAL presented to Acebrophylline or identical dosages of Arborol, explicit histochemical assessment strategies. Recognized a distinct expansion in Surfactant combination, especially in the cells presented to Acebrophylline.

2. **Bronchodilator Action**

Acebrophylline goes about as an enemy of cholinergic receptor. Its principal act is the M3 receptor-impeding activity. M3 receptor is a Gi sort of G-protein coupled receptor. At the point when Caryophyllene ties to the Gi-type receptor, Gross domestic product is changed over completely to GTP, and the alpha, beta, and gamma subunit get to disconnect from the receptors. Followed by alpha-GTP restricting to the adenylyl cyclase. Likewise, decline the type of cyclic AMP. There for arrival of the ca2+ particle this case the bronchial smooth muscle construction. In this process, Acebrophylline binds to the air conditioner interaction and blocks the cyclic AMP process likewise hinders the arrival of ca2+ particle, and experiencing the same thing k+ particle gets delivered in the bronchial smooth muscle which causes the bronchodilator activity Which impact delivers the bodily fluid to outside [3]

- Treatment of Acebrophylline**

Treatment for respiratory circumstances that as Bronchial asthma and ongoing obstructive Pneumonic sickness utilize a prescription called Acebrophylline. It is a xanthine subordinate with Broncho-lazy and mucoregulator properties. It Capabilities as bronchodilator to broaden the aviation routes What's more, further increment wind stream by loosening up the Smooth muscles in the aviation routes. It likewise has calming characteristics that lessen aviation route Aggravation and may forestall the development of Incendiary middle people. The mucoregulator Properties of Acebrophylline might be utilized to Control the development of bodily fluid in the aviation routes. It could make respiratory discharges less gooey, which would make expectoration and bodily fluid Leeway more viable. Patients with respiratory Conditions who use Caryophyllene inhale more straightforward, less hack oftentimes, and have less aggregate Intensifications. It could assist with side effects Counting wheezing, breathing issues, and chest Heaviness [4].

The impacts of Acebrophylline on sputum Creation, FEV indispensable limit (VC), and aviation route 1 Blockage were all fundamentally certain. Also, most of exploration has shown That Acebrophylline is more dynamic than Arborol In view of its more effective mucoregulator. Moreover, Acebrophylline essentially diminished the quantity of bronchospastic assaults Furthermore, was a better choice than theophylline. Is very much endured and has less Side reactions, as per a few preliminaries in grown-ups. The gooey flexibility of bodily fluid has moved along More recognizably with Acebrophylline than with Arborol, yet not altogether, making it more Liquid and decreasing the requirement for expectoration. Patients getting Acebrophylline showed huge upgrades in trial of respiratory Capability. Patients getting Acebrophylline didn't Report any cardiovascular issues, for example, Quakes, tachycardia, chest inconvenience, or Palpitations. The way that Acebrophylline has

a Lower recurrence of cardiovascular and CNS Unfriendly impacts might be on the grounds that it has a more prominent Blood convergence of the Arborol it contains than its xanthine subsidiary, which is connected to horrible side effects (5)

Advantages

- Pathogenesis of Mucus hyper secretion
- Conditions affected by Mucus hyper secretion/impaired mucus Clearance
- Long term effect of mucus hyper secretion if left untreated
- Importance of treating mucus hyper secretion
- Acebrophylline + N-Acetylcysteine
- Clinical evidence
- Guidelines/Recommendation for management.

Disadvantages

- You may experience side effects like drowsiness, dizziness, nausea, vomiting, stomach discomfort, diarrhea, constipation after taking Acebrophylline.
- It is often well accepted, and any adverse
- Effects, such as gastrointestinal issues,
- Headaches, dizziness, and skin rashes, are
- Typically, moderate and temporary.

Pharmacokinetics study of Acebrophylline

At the point when 200 mg of oral Acebrophylline is controlled to sound workers, the two Atoms that make up the compound Arborol Also, Theophylline-7 acidic corrosive are delivered in the Stomach and consumed there as well as in the Digestive system, where they arrive at their pinnacle. Convergences of Arborol and extremely low degrees of Theophylline-7 acidic corrosive. Theophylline-7 acidic Corrosive (mean Coax 0.008 mcg/mL) and Arborol (mean Coax 0.369 mcg/mL) both top after one Hour. Subsequently, apparently the last option is by the same token Ineffectively ingested or utilized rapidly and eliminated rapidly. Theophylline had in people, whose restorative Window compares to a lot more noteworthy plasma Focuses (10-20 mcg/mL). Acebrophylline Great bearableness is likewise due to some extent to its Pneumonic tropism. One more affirmation that there Ought not be any association with some other Theophylline-based meds that might be Directed simultaneously comes from the low Plasma levels of the xanthine subordinate. Acebrophylline just must be required two times every day Because of its strength in an acidic climate, great Tissue dissemination, and moderately lengthy half-life (6)

Clinical trials study

The viability of Caryophyllene and Arborol were thought about in two early clinical examinations. Silvio and Coat al. 41 patients between the ages of 30 and 80 who had intense asthma-like bronchitis or flare-ups of chronic types, with, with, with or without fever, expanded bronchial emission, cough, and bodily fluid, or mucopurulent or purulent sputum, were treated in a twofold dazed preliminary. For 20 days, patients were haphazardly doled out to get either Acebrophylline or Arborol (both at 200 mg b.i.d.). Sputum creation in the two gatherings had fundamentally diminished at the finish of the preliminary, and thickness had likewise altogether diminished, especially in the Acebrophylline -treated people. Be that as it may, Acebrophylline extensively raised FEV1 contrasted with Arborol by around 16% while the two treatments enormously decreased clinical symptoms.

Combination Therapies

Consolidating different classes of bronchodilators into a solitary treatment is a possibility for patients with Constant side effects and deficient administration of their respiratory sicknesses. Consolidating a few Prescriptions can lessen individual medication measurements, smooth out solution plans, diminish side Impacts, and lift consistence. Pharmacological Research proposes that joining drugs with various components is helpful. Contrasted with as of now accessible drugs, xanthine shows the possibility to further develop aftereffects essentially in rates, spirometry estimations, and prescription Consistence. The utilization of these meds in twofold Blends with each other or with other Respiratory medications might augment results while diminishing poison levels because of measurements. Moreover, it has been shown that Doxycycline Fundamentally further develops spirometry boundaries and decreases the necessity for salvage agonists in Respiratory issues including asthma and COPD. It has for the most part been utilized as an extra treatment to Support medications. Various examinations have shown that prescription mixes generally produce prevalent helpful outcomes than single agent medicines. Joining Doxycycline 400 mg With Acebrophylline 100 mg in a solitary portion to Treat COPD, bronchial asthma, and aspiratory Illness with spastic bronchial asthma is a decent Methodology to resolve the significant issue in the worldwide Populace and is more gainful than single medication Treatment, as indicated by surveys of the remedial Impacts and results of clinical preliminaries of Doxycycline and Acebrophylline [7].

Chemical and physical properties of Theophylline

- Is the model xanthine bronchodilator.
- A smooth muscle relaxant utilized for help of bronchospasm in specific respiratory circumstances:
- particularly aminophylline a subordinate of theophylline utilized in asthma and COPD.

- Has a thin helpful record.
- Eccentric digestion, affinity for drug responses and noticeable incidental effects.
- It is more dissolvable in water than theophylline.

Mechanism action of Theophylline

- 2 instruments hypothesized
- Restraint of Phosphodiesterase (PDE), which brings about an expansion in the intracellular convergence of cAMP and improved expulsion of calcium-smooth muscle loose.
- It follows up on adenosine receptors-alienate the impacts of adenosine.
- Adenosine enacts adenylate cyclase, which has cardiovascular depressant, bronchoconstrictor, favorable to incendiary and platelet-conglomeration suppressant impacts
- Theophylline loosens up the smooth muscles situated in the bronchial aviation routes and aspiratory veins. It likewise diminishes the aviation route responsiveness to receptor, adenosine, methacholine, and allergens. It applies these impacts for the most part through two unmistakable instruments:
- Theophylline seriously restrains type III and type IV phosphodiesterase (PDE), the catalyst answerable for separating cyclic AMP in smooth muscle cells, perhaps bringing about bronchodilation. Theophylline likewise ties to the adenosine A2B receptor and blocks adenosine interceded bronchoconstriction.
- Theophylline causes an expansion in the centralization of cAMP in the cell through hindrance of phosphodiesterase-3 and 4. As with the β_2 agonists, an expansion in cAMP fixation drives eventually to a diminishing in accessible calcium in the cell and smooth muscle unwinding.

Role of Theophylline in Chronic Obstructive Pulmonary

Theophylline is a medication removed from a purine derivative (1, 3-dimethylxanthine) and is naturally present in tea, cocoa, and beans. It was one of the medications prior utilized for the treatment of asthma, initially as aminophylline both in oral and intravenous structures. This medication had an extremely limited helpful window as portions utilized around then for bronchodilation, were likewise connected with serious gastrointestinal, heart, and focal apprehensive system (CNS) unfavorable impacts. Seizures, cardiovascular arrhythmias, and even mortality were likewise seen when blood concentrations became too high due to pharmacokinetic communications. Accordingly, theophylline acquired ubiquity with the accessibility of supported discharge items and business computerized examines that permitted helpful blood level monitoring. However, the utility of theophylline declined when breathed in bronchodilators were presented since the beyond couple of many years. Theophylline is generally endorsed at lower fixations in light of its anti-inflammatory effects in COPD and is a more secure choice presently than before. It generally goes about as smooth muscle relaxant located in the bronchial airways and pulmonary blood vessels.(8).It likewise diminishes the aviation route responsiveness to various agents such as histamine, adenosine, methacholine, and allergens. There are two significant pharmacological systems of activity for theophylline which incorporate expansive range. DE restraint prompting expansion in the convergence of Intracellular cyclic adenosine monophosphate and guanosine Monophosphate, enactment of protein kinase A, hindrance of cancer putrefaction factor alpha and leukotriene blend What's more, another adenosine receptor adversary prompting Anti-inflammatory effects.

Dose-dependent harmfulness is noticed for example, gastrointestinal

Advantages of theophylline

- The job of theophylline in COPD is disputable.
- Theophylline gives no extra bronchodilator impact past that of beta agonists or anticholinergics.
- Then again, long-acting arrangements might lessen for the time being decreases in aspiratory capability and further develop morning side effects.
- This helpful reaction to theophylline to forestall diaphragmatic weakness, animate conciliary freedom, increment the focal reaction to breath, and lessen aviation route
 - Aggravation.
- Supported discharge arrangements are generally fitting for the drawn- o u t administration of COPD, they enjoy the benefits of working on tolerant consistence and
 - accomplishing more predictable serum focuses over fast delivery theophylline and aminophylline arrangements
- Try not to switch brands.

Disadvantages of theophylline

- Its incidental effects are more different and May incorporate sickness, quakes, Headaches, stomach-related issues, and an Expanded pulse.
- Huge Antagonistic impacts including arrhythmias or spasms could happen with high Measurements.
- Hypersensitivity which might life undermine.
- Serum ailment: fever, arthralgia, rash.

- Eosinophilic conditions: eosinophilia, vasculitis rash, deteriorating respiratory side effects.
- Commonest responses: arthralgia, torment, weariness, discombobulation, migraine.
- Infusion site responses: redness, warmth, bumming sensation. These for the most part at ensuing portions.
- Harm: was seen in clinical examinations.

Pharmacokinetics study of theophylline

Theophylline has tracked down acknowledgment as an intense bronchodilator and as a significant specialist for the prophylactic Concealment of persistent asthma side effects. This has not Continuously been valid. During the sixties, a letter from an incensed, Notable allergist about our utilization of theophylline for a Patient as of late released from the Public Asthmatic Focus confounded us [19, 20]. The doctor expressed he was Quickly subbing prednisone for the theophylline. We were unable to comprehend the reason why he would involve such a possibly perilous drug for one that we considered the backbone of our treatment. We shouldn't have been Shocked on the grounds that, in the 1960's, theophylline was thought of as by a lot of people to be a hazardous and poisonous drug. Its utilization through the 1950's and 1960's left an area of Dreariness and mortality the country over. Since that Time, theophylline has gone through many patterns of purpose, Misuse, dismissal and afterward restoration with resurgence in Usage in view of as of late characterized pharmacologic understanding. Methyl xanthine's were first proposed in the treatment of asthma toward the finish of the nineteenth century when it was Prescribed to take two cups' areas of strength for of for Asthma side effects and was recommended to forestall work out Actuated bronchospasm. It was only after the start of the fourth 10 years of this century that the most powerful Bronchodilator in the methyl xanthine class, theophylline, was presented for use in intense and ongoing asthma [18]. In 1937, the treatment of status with intravenous aminophylline was proposed and by the 1940's, an oral planning was joined with the main other successful oral Medicine around then, ephedrine, in a proper portion relationship of five sections theophylline to one section ephedrine. The proportion was laid out more out of show than in light of authentic exploration. The proper portion mix Turned into the most famous available albeit numerous Various definitions and salt arrangements were utilized to Increment solvency. Since oral theophylline was felt to be Too inadequately consumed, giving just low blood levels, the Makers created a rectal suppository which was Remembered to be more solid because of its more noteworthy retention and this before long prompted the defeat of theophylline due to its poisonousness [17]. Not many investigations at the time reported the Genuine adequacy of theophylline. With the utilization of both oral Furthermore, rectal theophylline, various passing's were credited to this medication. Notable clinicians of the day Implicated the utilization of theophylline as the guilty party for Expanded dismalness from asthma and recriminations in noticeable diaries implicated the blend with Ephedrine [9].

Combination Therapies of theophylline

Theophylline in stable COPD patients who were receiving regular Doses of salbutamol.

Subject Selection

Subjects with a clinical determination of COPD, stable pneumonic Capability, getting salbutamol and a long-acting theophylline planning were incorporated. The review got morals board endorsement, and informed assent was acquired from each subject. People with a clinical determination of asthma or with an improvement after bronchodilator of more noteworthy than 15% in constrained Expiratory volume in one moment (FEV) or constrained imperative limit (FVC) were avoided. Those with suggestive arrhythmias and Those getting antiarrhythmic prescription was also excluded. Cur Pulmonology, cardiovascular infection, and the presence of arrhythmias on a Resting ECC were not without help from anyone else prohibition measures [15, 16].

Study Population

We contemplated 25 subjects (four ladies and 21 men) whose mean age Was 65 ± 8 . Mean standard FEV. Was 31 ± 13 percent of anticipated, FVC 60 ± 18 percent of anticipated, mean FEV/FVC proportion 38 ± 12 Percent. Mean pH was 7.41 ± 0.05 ; Poe., 42.9 ± 9 ; POI' 68.4 ± 14 . Fifteen subjects had simple COPD, five subjects showed Proof of cur pulmonology in light of actual assessment, chest x-beam film, or ECC. Five different subjects had proof of stable coronary course illness. A solitary individual showed incidental PVCs on the standard ECC.

Protocol

Subjects were assessed at pattern, while getting both theophylline and salbutamol (assessment T1) after the portion of theophylline had been changed in accordance with accomplish serum levels in the remedial reach (10 to 20., glumly). Theophylline was then supplanted by Fake treatment and a recurrent assessment was played out a normal of 48 Hours after the fact (assessment P). Dynamic theophylline was then continued and the patients reexamined for the last time (assessment T2) after steady State serum theophylline levels were in the remedial reach. During the whole-time frame of the study, members were told to keep on taking salbutamol multiple times every day at the typical portion.

Three subjects on T1 and four subjects on T2 had Theophylline levels underneath 9.0 IJ. G1ml. Measurable correlations were Performed both when rejection of the information for those review Days. As this didn't adjust the factual meaning of any examination, the information from these assessments is remembered for all results shown. Halter accounts were finished with a double ECG channel recorder Model 4-24. Skin cathodes were set to acquire changed Val and V5 leads for ensuing examination. The Halter accounts were investigated by experienced faculty dazed to the review convention. A Reynolds Pathfinder analyzer and pattern framework was used [13].

Tapes Were assessed subjectively and quantitatively for pulse (HR), Ventricular ectopic beats (PVCs), ventricular couplets, runs of Ventricular tachycardia (i.e., at least three successive beats), supraventricular extra systoles (SVPCs), and runs of supraventricular Tachycardia (i.e., at least three successive beats). Likewise, pattern Investigation of supraventricular and ventricular ectopic beats was finished [14].

Statistical analysis

Arrhythmia recurrence data were standardized by log (n+1) transformation before factual investigation to make up for the intrinsic Scenes of arrhythmia recurrence information [42]. Group outcomes for the three Assessments T1, and T2 were examined utilizing two-way investigation of Fluctuation (ANOVA). The Newman-Keels technique was then utilized for Correlation of sets of gathering implies if a massive distinction between bunches was found by ANOVA. Results were considered to Be measurably critical when p was under 0.05. Individual reproducibility of arrhythmias on Halter accounts was surveyed involving straight relapse investigation as beforehand described [10].

A new Bronchodilator and Anti-Inflammatory Agent: Acebrophylline

A new bronchodilator with mucosectomy and Anti-Inflammatory properties, Acebrophylline is used to treat asthma, bronchospasm, and COPD. Oral bronchodilators are frequently recommended. On a clinical level, Acebrophylline is therapeutically effective in patients suffering from acute or chronic bronchitis, chronic obstructive pulmonary disease, and asthma. It functions by lowering the frequency of bronchial obstruction episodes increasing the amount of beta agonists. and enhancing ventilatory function [11,12].

Conclusion

Currently, there is no cure for asthma or COPD, and new medications are always being developed. These conditions are also not well understood. As with Theophylline, acebrophylline is a brand-new, off-the-shelf xanthine derivative drug that treats respiratory conditions. Acebrophylline has been shown in multiple clinical investigations to be safer than Theophylline due to its less side effects. But a recently developed drug called doxycycline has anti-inflammatory, bronchodilator, and microregulating qualities. The moderateness, viability, and sufficient bearableness profile of doxycycline make it a recommended additional medication. More negative effects on the neurological and circulatory systems are likely to occur with theophylline than with acebrophylline. For the treatment of certain respiratory conditions like COPD and asthma, Bubo Health (Hilt Brands India Pvt Ltd) offers the Brookite Stomach Muscle SR 200, an Acebrophylline assisted discharge pill. Following this logic, it is reasonable to conclude that: 1) Methylamines are a very viable adjunct therapy to inhaled tentorium for the management of moderate COPD. The improvement of spirometry parameters and the indication of benefit for individuals with COPD are equivalent between Caryophyllene and Supported Discharge Theophylline. It is also evident that acebrophylline is safer than SR Theophylline with respect to side effects connected to the cardiovascular and focused sensory systems.

Author contributions

All authors are contributed equally.

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Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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