

A Review - Carisoprodol as Skeletal Muscle Relaxant

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ABSTRACT

In the world of pharmacology, the prescription of a medicine and its dosage play important role. Different physico-chemical methods are in vogue in describing the interactions of the drug molecule with host target among them, the chief being spectroscopic, chromatographic and quantum mechanical techniques. Skeletal muscle relaxants are divided into two categories: antispastic (for conditions such as cerebral palsy and multiple sclerosis) and antispasmodic agents (for musculoskeletal conditions). Antispastic agents (e.g., baclofen [Lioresal], dantrolene [Dantrium]) should not be prescribed for musculoskeletal conditions because there is sparse evidence to support their use. Rather, an antispasmodic agent may be more appropriate. Many of the studies evaluating the effectiveness of skeletal muscle relaxants are hampered by poor methodologic design, including incomplete reporting of compliance, improper or no mention of allocation concealment, not utilizing intention-to-treat methods, and inadequate randomization. Skeletal muscle relaxants have been evaluated in systematic reviews and meta-analyses. These include Methocarbamol, Meprobamate, Metaxalone, Carisoprodol, Dantrium and Baclofen. Chemically Carisoprodol is N-isopropyl-2-methyl-2-propyl-1,3-propanediol dicarbamate. Methods like nitration, Sulphonation, Methylation, Esterification, Acetylation and Diazotization was used for formation of new derivative which can be detected in UV region. Different reactions of diazotization were used for getting a new and novel derivative of Carisoprodol. Physicochemical properties, TLC, UV, IR and NMR analysis of Carisoprodol and newly obtained derivatives of Carisoprodol was studied and it showed that there was change in color, odour, taste, melting point, solubility pattern of original drug and derivatives.

Keywords : Carisoprodol, Diazotization, Derivatization, Spectroscopy.

I. INTRODUCTION

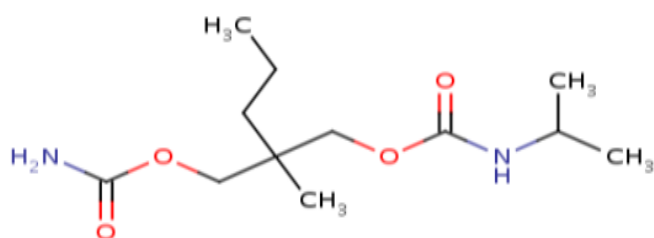
Strains, sprains and other muscle injuries can result in pain, stiffness and muscle spasms. Muscle relaxants do relax muscles ease discomfort and stop muscle spasms. Muscle pain is the characteristic feature of several conditions. For example, in certain viral fevers such as Chicken guniya, the patient experience severe muscle pains. Similarly in case of arthritis, the patient will be thrown into discomfort initially and may become disable in severe condition. People belonging to risky

jobs in various fields such as workers in mine, software engineers suffer from joint pains and severe chronic back pain.

The discovery of central acting muscle relaxants dates back to 1910. Berger and Bradely in 1946, observed the muscle relaxant activity present in large number of glycerol mono ether and analogues. Skeletal muscle relaxants consist of both anti spasticity and spasmodic agents. Approximately 2 million people per year report using a skeletal muscle relaxant, primarily for

back pain, with an estimated 3,00,000 of the patient being elderly. Spasmolytic agents generally work by either enhancing the level of inhibition or reducing the level of excitation. The benzodiazepines, such as diazepam, interact with the GABA receptor in the central nervous system and Baclofen is considered to be an effective as diazepam in reducing spasticity and cause much less sedation. Dantrolene is a spasmolytic agent with a unique mechanism of action outside the CNS other common spasmolytic agents include Methocarbamol, Carisoprodol, Chlorzoxazone, Metaxalone and Orphenadrine. Meprobamate, a potent adenosine reuptake inhibitor and related drugs include Carisoprodol and Tybamate A centrally acting skeletal muscle relaxant whose mechanism of action is not completely understood but may be related to its relative actions. It is used as an adjunct in the symptomatic treatment of musculoskeletal conditions associated with painful muscle spasms

Structure: Molecular structure of Carisoprodol is presented in Fig



Mechanism of Action: Carisoprodol is a central nervous system depressant that act as a relative and skeletal muscle relaxant. Carisoprodol interrupts neuronal communication within the reticular formation and spinal cord, resulting in radiation and alteration in pain perception. Its exact mechanism of action is not yet known.

Indications: For the relief of discomfort associated with acute, painful, musculo skeletal conditions.

Toxicity: Symptoms of over dose include drowsiness, giddiness, nausea, indigestion, or rash. Other adverse effects attributed to therapeutic use of Carisoprodol

include dizziness, irritability, insomnia, diplopia, temporary loss of vision, ataxia, weakness, headache and dysarthria.

Carisoprodol is skeletal muscle relaxant. The centrally acting muscle relaxant carisoprodol has been on the market for >40 years¹. It widely used skeletal muscle relaxant and analgesic and is available as a prescription drug and by blocking interneuronal activity in the descending reticular formation and spinal cord and as an analgesic. Single oral dose of 350 mg Carisoprodol with the onset of action occurring at 0.5 hours and duration of 4 to 6 hours. The peak serum concentration is 4 to 7 µg/mL; the half-life is 8.0 hours.

In many instrumental techniques, it might be desired to assay particular compounds in forms that are readily handled to improve sensitivity or selectivity. Usually conversion of functional groups within the molecule to others more readily adaptable to the technique at hand is preferred. This procedure called derivatization or derivative formation is applied in UV spectroscopy, gas chromatography (GC) and high performance liquid chromatography (HPLC).

II. METHODS AND MATERIAL

Derivatization technique:

The derivatization mantra has been that, for the technique to be worthwhile, it selective, and that the derivatizing reagent should react quantitatively with the analyte and only give one final product. Derivatization is the process by which a compound is chemically changed, producing a new compound that has properties more amenable to a particular analytical method. Compounds that have poor volatility, poor thermal stability, or that can be adsorbed in the injector will exhibit non reproducible peak areas, heights, and shapes. Other compounds that respond poorly on a specific detector may need

to be “tagged” with a different functional group to improve detection. Pharmaceuticals can be classified into inorganic, organic compounds as well as excipients.

The need to have a readily adaptable method for the quality control of these compounds has led to the development of a wide range of reactions and procedures. Majority of these pharmaceuticals lack adequate chromophores which can permit analysis at wavelength regions beyond the nonspecific UV-region of the electromagnetic spectrum. Thus derivatization reactions are carried out to convert these pharmaceuticals to readily determinable compounds whose properties and concentrations can be related to the original compound.

Reasons to Derivatization

The primary reasons to wish to incorporate a derivatization step as part of the extraction methodology into the analytical analysis is one or many of the following: to enhance separation, to change solubility, to increase selectivity for a particular analyte, for enhanced thermal stability, to maintain speciation, to fix the oxidation state of a metal, and to attach a particular selective label for use with a specific detector. As one example, mono-hydrogen-substituted thiols can be preferentially detected and quantitated from di-thiol compounds (e.g., thiophene) in complex petroleum tar sand by the use of the N-phenylmaleimide derivatizing reagent. Often, derivatization can increase sensitivity for a particular component by several orders in magnitude, as has been shown in the study of human health, by using a trimethyl silylation derivatizing reagent (TMS) for monitoring metabolism in fecal water, followed by subsequent GC/MS analysis.

Methods and Conditions for Derivatization

1. Solvent Considerations for Derivatization, Extraction, and Sample Preparation
2. Solvents for silylation¹⁶

3. Other common solvent considerations for derivatization reagents¹⁷⁻¹⁸

The nitrosation of primary aromatic amines with nitrous acid (generated in situ from sodium nitrite and a strong acid, such as hydrochloric acid, sulfuric acid, or HBF₄) leads to diazonium salts, which can be isolated if the counterion is non-nucleophilic. Diazonium salts are important intermediates for the preparation of halides (Sandmeyer Reaction, Schiemann Reaction), and azo compounds. Diazonium salts can react as pseudohalide-type electrophiles, and can therefore be used in specific protocols for the Heck Reaction or Suzuki Coupling. The intermediates resulting from the diazotization of primary, aliphatic amines are unstable; they are rapidly converted into carbonations after loss of nitrogen, and yield products derived from substitution, elimination or rearrangement processes.

III. RESULTS AND DISCUSSION

EXPERIMENTAL WORK

Material and Chemicals

Instrument used was an UV/Visible double beam spectrophotometer, SHIMADZU model 1800 (Japan) with spectral width of 2 nm, wavelength accuracy of 0.5 nm and a pair of 10 mm matched quartz cell was used to measure absorbance of all the solutions.

An electronic analytical balance was used for weighing the sample. Melting point taken on thiele's tube apparatus and are uncorrected. Thin layer chromatography was used to assess the course of reaction and the purity of the intermediates and the final compounds. All the chemicals and solvents were using are of A.R. grade.

METHODS:

- 1] Diazotization²⁶⁻²⁷
- 2] Sulphonation²⁸
- 3] Nitration²⁹
- 4] Methylation³⁰

EVALUATION OF PRODUCTS:

Evaluated by physiochemical characteristic, TLC, UV spectral analysis, IR studies and NMR interpretation. Color was observed visually while taste was evaluated and solubility behavior of all derivatives was studied using different solvent.

1. Melting point determination
2. Thin layer chromatography
3. Ultraviolet (UV) spectrophotometer determination
4. Infrared (IR) determination

Discussion:

Derivatization offer an excellent method in producing a product which can be used to overcome the analytical problem occurs during the analysis of drug. Derivatization proves advantageous for many polar compounds and samples that are not suitable for chromatographic analysis due to their physical and chemical properties. Derivatization promises to be a potential approach for many compounds.

So this study highlights the need of derivatization for the compounds which shows problems in analysis. Derivatization of carisoprodol was conducted by using diazotization, sulphonation, nitration, and methylation and esterification process.

Some methods of derivatization were conducted but diazotization was preferred for formation of derivatization. Physiochemical properties, TLC, UV spectral analysis, IR and NMR analysis of carisoprodol and derivatized product obtained of carisoprodol was studied and it was found there was change in color, odour, taste, melting point, TLC, UV spectrum, IR and NMR analysis pattern of original drug and derivatized product. So this study highlights that

diazotization is most suitable methods for derivatization of carisoprodol.


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