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Etomidate Analogs: State of Development

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ABSTRACT: As an anesthetic agent, etomidate provides profound hemodynamic stability, superior to propofol even when it is dose reduced. However, its use has been curtailed due to concerns regarding adrenal cortical suppression demonstrated clinically in the setting of prolonged infusion for sedation in the intensive care unit. In addition, etomidate reproducibly results in significant myoclonus when employed in the absence of other pharmacology. Recently, utilizing both pharmacokinetic and pharmacodynamic considerations, a number of etomidate analogs have been developed that retain the favorable properties of their parent agent, including rapid onset of hypnosis and rapid recovery, amnesia, and cardiovascular stability, but do not result in inhibition of steroidogenesis. A few of these analogs have now entered clinical trials and are poised to transform acute care and anesthesia for critically ill patients.

Keywords: Etomidate analogs; Adrenal suppression; Drug design; ET-26; ET-42

Provision of general anesthesia is necessary in critically ill patients with limited cardiovascular (CV) stability during emergencies, diagnostic interventions, or therapeutic procedures requiring advanced cardiopulmonary support. This relative instability may result from issues related to low cardiac output (such as limited stroke volume due to low preload, impaired contractility, and/or increased cardiac afterload) and/or low systemic vascular resistance (related to sepsis, anaphylaxis, pharmacology, or another systemic condition). In these settings, one intravenous hypnotic with significant CV stability is etomidate [1,2]. Unlike propofol, this medication does not significantly decrease myocardial contractility or vascular sympathetic tone and preserves autonomic reflexes [3,4]. As such, arterial blood pressure usually remains largely unchanged during use of etomidate for the induction of general anesthesia or for intravenous sedation [1,3,5,6].

Unfortunately, the use of this medication for the induction of anesthesia in critically ill patients has been limited by its transient biochemical effect on adrenal steroidogenesis that occurs approximately 80% of the time in some settings [7], and by the clinical effects related thereto involving increased mortality in the setting of continuous infusions delivered over days in the intensive care unit [4,6,8,9]. This adverse effect is likely due to inhibition of the enzyme 11beta-hydroxylase, resulting in diminished cortisol production. Notably, short-term glucocorticoid coverage is usually relatively benign, although its effect on altering clinical outcome in the above setting may not be significant [10]. However, despite this consideration and although similar negative clinical outcomes have never been demonstrated from single bolus administration to induce general anesthesia (its predominant role now that etomidate is rarely employed as a continuous infusion to sedate patients in the ICU) [2,11], this potential problem has led to

concerns that have limited etomidate's usage despite its utility [12,13]. The wisdom of this limitation remains controversial and may reflect the complex interplay of multiple factors in determining outcome in critically ill patients.

While the relative clinical risks of etomidate bolus versus continuous administration are likely different [12], because etomidate has been associated with increased mortality among critically ill patients, etomidate analogs (EAs) have been developed [1,2]. EAs constitute a large number of similar compounds that have been produced and studied to varying degrees in an attempt to develop compounds that retain the desired properties of etomidate without its adverse effects. These desired properties include a rapid intravenous hypnotic effect with rapid recovery, profound amnesia, CV stability, and a cerebroprotective effect [2,14]. Undesirable adverse effects of etomidate include impaired adrenal steroidogenesis, pain with intravenous injection, lack of analgesia, nausea and vomiting—unlike propofol, which has direct antiemetic properties—and myoclonus or myoclonus-like involuntary skeletal muscle movements (IMM) [2,13].

Such IMM is related to epileptiform activities and occurs frequently with induction doses of etomidate in unpremedicated patients, with an incidence of 50–80%. It can be associated with multiple types of adverse events. These include vitreous prolapse after open-globe injury, aspiration associated with increases in intragastric pressure, especially in inadequately fasted or emergency patients, and blood pressure spikes with increases in myocardial oxygen demand [15].

Among these undesirable effects, eliminating or minimizing problems associated with steroid synthesis has been the focus of most initial efforts in EA development. This course of action may be related to the fact that pain during etomidate administration can be minimized by using a lipid emulsion rather than propylene glycol as a stabilizer [16] and that the drug is commonly administered during anesthetic induction, thereby eliminating myoclonus associated with bolus initiation of general anesthesia. Pretreatment with other sedatives, including dexmedetomidine, opioids, or midazolam, also reduces or eliminates IMM during use of etomidate infusions [15,17].

To maintain the desired properties of etomidate but eliminate problems associated with inhibition of steroidogenesis, researchers have focused on both pharmacokinetic and pharmacodynamic considerations [18]. Termination of hypnosis due to a single intravenous bolus of etomidate is rapid via redistribution from the central nervous system compartment—although with repeated dosing or infusions, peripheral compartments fill, resulting in context-sensitive prolongation of effect [19]. However, etomidate and some EAs can maintain an adverse adrenal effect for days, and therefore EAs with ultra-rapid degradation by nonspecific plasma esterases were identified [3,6].

1. CPMM (ABP-700)

The story of the development of the current generation of EAs involves a concerted effort to build a drug that maintains the beneficial pharmacokinetic and pharmacodynamic properties of etomidate without its adverse effect on steroidogenesis and involves optimally rapid degradation to inactive metabolites [20]. One such is cyclopropyl-methoxycarbonyl-metomidate (CPMM; also known as ABP-700, as administered by Apexigen during its use in clinical trials [6]; Table 1). It is formulated as a 10% solution (10 mg/mL unlike etomidate, which comes as a 2 mg/mL or 2% formulation), and bolus administration of 0.25–0.35 mg/kg induces hypnosis consistent with general anesthesia similar to etomidate [6].

Table 1. Etomidate Analogs.

Analog	Molecular Formula
Etomidate	$C_{14}H_{16}N_2O_2$
Carboetomidate	$C_{15}H_{17}NO_2$
MOC-Etomidate	$C_{16}H_{18}N_2O_4$
CPMM (AB-700)	$C_{17}H_{18}N_2O_4$

ET-26	$C_{14}H_{16}N_2O_3$
ET-42	$C_{17}H_{22}N_2O_3$
EL-0052	$C_{14}H_{15}FN_2O_2$

CPMM derives from methoxycarbonyl-carboetomidate (MOC-carboetomidate), an EA that combines the favorable characteristics of both methoxycarbonyl-etomidate (MOC-ET) and carboetomidate. The creation of MOC-ET initially involved the addition of a new ester moiety RCOOR′, where "R" and "R′" represent hydrogen atoms or alkyl groups (Table 1). This group is prone to rapid hydrolysis by serum esterases, which also prevent tight binding to the hydrophobic catalytic site of 11beta-hydroxylase and lead to concurrent adrenocortical suppression [21]. However, because of this ultra rapid metabolism, large quantities of parent drug become necessary to induce anesthesia, and increased amounts of (markedly less potent) metabolites, such as methoxycarbonyl-etomidate carboxylic acid (MOC-ECA), associated therewith significantly delay recovery [2].

Multiple derivatives of MOC-ET were developed in an attempt to slow this ultra-fast process. Alternatively, carboetomidate, the other parent compound of CPMM, was formulated by designing out the imidazole ring of etomidate that interacts with the 11beta-hydroxylase (Table 1). This EA demonstrated significant promise related to its pharmacokinetics. It produced lower levels of metabolites (thereby avoiding prolonged awakening), such as the carboxylic acid of CPMM (CPMM-CA), that are not active in producing hypnosis at physiologic concentrations [22].

Early studies of CPMM were promising and demonstrated both retention of etomidate's favorable pharmacologic profile, including its hemodynamic stability, high hypnotic potency, and rapid onset, and showed markedly decreased affinity for cytochrome p450 11beta-hydroxylase (and therefore much reduced adrenal suppression) [6]. This diminished effect on adrenal steroidogenesis (first solved in the development of MOC-ET [3]) relates to the substitution of the nitrogen of etomidate's imidazole ring with a methylene group (Table 1), thereby rendering tight binding of the enzyme less favorable [3]. Furthermore, these properties were evident after both bolus induction and prolonged anesthetic infusion, a phenomenon likely related to low active metabolite brain concentrations [6].

In animal models, CPMM infusions showed an adrenocortical recovery profile similar to propofol [6]. Unfortunately, although CPMM appeared to be the most promising EA developed over a decade ago because of these pharmacodynamic and pharmacokinetic properties, use of this agent in experimental models has been limited by an increase in IMM that can occur with high frequency in some settings [15,23]. Of note, however, when used in combination with other medications, this adverse and clinically unacceptable effect can be mitigated pharmacologically [6], albeit at the cost of complicating the anesthesia and adding some degree of variability. An ideal EA would demonstrate pharmacokinetics and pharmacodynamics similar to CPMM but without IMM.

2. ET-26 and ET-42

Because of such IMM, other EAs—notably ET-26 (methoxyethyl etomidate) and ET-42 (methoxy-2-methylpropyl etomidate)—were developed (Tables 1 and 2) [13]. Like CPMM, these EAs retained the hemodynamic-stabilizing effects of etomidate, as well as many elements of its desirable pharmacokinetic profile, while minimizing adrenocortical suppression by lacking inhibition of 11beta-hydroxylase. To date, ET-26 has been studied in Phase-II clinical trials [13] and its pharmacokinetics has been defined in animals [24] and in humans [25,26], whereas the largely investigational agent ET-42 has been studied in animals only [24]. Both EAs appear to undergo rapid redistribution from the CNS to terminate their hypnotic effect with comparatively slower metabolism to biologically inactive products that do not produce hypnosis at physiologic doses or significantly inhibit steroidogenesis [13,24–26].

Table 2. Comparison of ET-26 and ET-42.

Feature	ET-26	ET-46
CV Stability	Excellent	Excellent
Adrenal Suppression	Minimal/None	Minimal/None
Pharmacokinetics	Rapid Onset/Short Duration	Rapid Onset/Short Duration
Metabolism	Slow to Inactive Metabolites	Slow to Inactive Metabolites
Myoclonus-like Movements	Controversial	Unknown
Hypnotic Potency	1/3 Etomidate	1/2 Etomidate
Development Status	Clinical (Phase III)	Pre-clinical

However, unlike CPMM, ET-26 and possibly ET-42 may cause little IMM, although the data is controversial, with different studies citing markedly different incidences of this adverse effect [2]. ET-26 also has a low incidence of nausea/vomiting [26]. These agents have reduced and different anesthetic potencies compared with etomidate (one-third and one-half, respectively). For example, the induction dose of ET-26 in early clinical experience was 0.8 mg/kg, compared with 0.3 mg/kg for etomidate.

3. ET-26—The Most Promising EA

Although ET-42 is pharmacodynamically closer to etomidate, its use is largely experimental. There is no human data for ET-42 [2]. ET-26, on the other hand, is a clinically more advanced EA candidate, although significantly less potent than etomidate. For this reason, together with its relative lack of inhibition of steroidogenesis and CV stability, it may be particularly useful in the near future for critically ill patients [19]. It actually demonstrated "superior myocardial performance" versus etomidate in some studies as defined by "echocardiography, ventricular repolarization, proarrhythmic risk and electrophysiology assessments" [27]. ET-26 is currently in phase III clinical development, and it seems to have achieved the goals set out for EA drug development [13,28], although the incidence of IMM with this EA needs clarification (see above [2]).

Only in the setting of brief procedural sedation do the pharmacokinetics of CPMM make it a superior choice to ET-26. ET-26 manifests a slightly longer duration of hypnotic effect versus analogs like CPMM. This comparatively less vibrant wake-up may be problematic, especially for short procedures [2]. But CPMM—possibly unlike ET-26—is troubled with significant IMM. As such, ET-26 remains the most promising EA for both bolus induction of anesthesia and continuous infusion for maintenance of anesthesia and for ICU sedation.

4. Propofol Replacement?

Due to its more rapid metabolism and somewhat shorter duration of action versus propofol, maintaining a specific depth of anesthesia for a prolonged time (key to successful minute-to-minute titration of anesthetic depth via infusion) is more difficult with ET-26. Unlike propofol, this pharmacokinetic property of ET-26 makes it less than ideal for total intravenous anesthesia (TIVA) or long-term continuous infusions [29,30]. As such, although significantly superior to propofol in terms of CV stability in patients with underlying circulatory compromise (even with propofol dose reduction), ET-26 is unlikely to replace propofol for anesthesia in patients with relatively normal hemodynamics.

Furthermore, the human data concerning ET-26 originate from preclinical studies or early clinical trials involving a limited number of patients that examined the efficacy and safety of this EA. The latter endeavors are Phase I single-center, non-randomized, single-blind investigations [25,26] that addressed the question of whether the drug is safe, and Phase IIa and IIb multicenter, randomized, single-blind investigations that established that ET-26 works well as a general anesthetic induction agent, providing conditions for successful tracheal intubation in healthy patients within minutes [26]. That is, the Phase II clinical trials established proof

of concept for ET-26 and defined dose-response relationships in patients. Other experience with this EA largely involves observations of its pharmacokinetics and pharmacodynamics in animals.

While these findings are encouraging, they do not yet demonstrate superiority in clinically meaningful outcomes. Multicenter, randomized, double-blind Phase III clinical trials with large patient samples are needed and are underway for this purpose [2,26]. At present, although promising, there is insufficient patient evidence to conclude that ET-26 should be considered superior to existing agents, including ketamine (an N-methyl-D- aspartate [NMDA] receptor antagonist with potent analgesic and hallucinogenic properties) and propofol.

Additionally, since its introduction into clinical practice more than a quarter century ago, propofol has developed a much-deserved reputation for safety and context-sensitive recovery with predictable performance and awakening even after extended infusions. This reputation has enhanced propofol's use among interventionists and other anesthesia providers. See Table 3 for a side-to-side comparison of these two anesthetic agents.

Table 3. Comparison of Propofol and ET-26. * Phase I and Phase II clinical trial data are only available.

Feature	Propofol	ET-26 *
Clinical Status	Widespread Use	Phase III Trials
Onset of Hypnosis	Rapid	Rapid
Duration of Hypnosis	Rapid Onset/Short Duration	Rapid Onset/Short Duration
Hemodynamics	Hypotension in Critically Ill	CV Stability
Titratability	++	+
Primary Advantages	Rapid, Predictable Recovery	Hemodynamic Stability

As such, ET-26 and other EAs may function as complements to propofol in specific clinical settings rather than as replacements. A hypothetical propofol replacement may be represented by a CPMM-like EA with pharmacokinetic characteristics that allow for easy, predictable titration but without associated IMM that occur commonly with etomidate and CPMM. But even such a theoretical entity faces the obstacles of propofol's history of reliability and usual clinically safe profile, much as propofol faced similar obstacles with thiopental, a short-acting barbiturate used extensively in previous years for induction of anesthesia with a fundamentally different mechanism of action involving different secondary receptors versus propofol, an alkylphenol [31].

Perhaps a more constructive and reasonable approach, then, is the use of EAs—not to replace propofol—but rather as potential complementary alternatives intended for specific patient populations in clinical scenarios where the use of propofol may be suboptimal. This distinction is important and reinforces the understanding of propofol's safety in most clinical situations. It also emphasizes the benefit of drugs that provide an added measure of CV stability for critically ill patients.

5. Past and Current Challenges

The current generation of EAs, including ET-26 and other novel EAs such as EL-0052—the latter agent with preclinical studies in animals showing similar hypnotic potency to etomidate, profound CV stability, and no significant adrenocortical suppression [32]—may represent complementary alternatives to propofol and ketamine in critically ill patients with limited CV stability, provided Phase III clinical trial data support this conclusion [1]. The road to their development has demonstrated the possibility of new anesthetics arising from computer-aided drug design and in silico screening [33]. This road has been difficult for a number of reasons including: (1) the same imidazole structure (a planar, five-membered heterocyclic compound containing two nitrogen atoms) contributes to etomidate's hypnotic efficacy and binds 11beta-hydroxylase to inhibit steroidogenesis; (2) design strategies created new problems: rapid

metabolism of MOC-etomidate resulted in accumulation of active metabolites and such rapid metabolism resulted in a need for higher doses that worsened such accumulation; (3) development of inactive-metabolite EAs caused loss of ultra-short kinetics; and (4) achieving a propofol-like context-insensitive half-time has been problematic with excessively fast metabolism requiring additional drug and excessively slow metabolism resulting in delayed recovery and metabolite accumulation [2]. Furthermore, reliable pharmacokinetic-pharmacodynamic modeling of etomidate and EAs has been limited [6].

As such, current challenges in EA development remain to optimize the positive characteristics of etomidate, including its CV stability, high hypnotic potency, and favorable pharmacokinetics allowing for titratable and predictable infusions, and avoid adrenal suppression, IMM, and other adverse effects common to this drug class. These drug properties need to be clearly demonstrated in properly designed Phase III clinical trials. Investigations with difficult endpoints, conflicting data, and heterogeneous patient populations (e.g., healthy versus critically ill patients) complicate this process. In addition, there are formulation and delivery problems related to stability and infusion compatibility, and economic and industry factors since EAs must justify their higher initial cost (higher than propofol or etomidate, which are both generic and relatively cheap at this time) and associated regulatory risk [2].

However, to a reasonable degree of certainty, ET-26 and similar medications will enter the clinical arena in the future. With their introduction into practice, these EAs will largely make the debate over whether bolus administration of etomidate is clinically safe a non-issue. Furthermore, they may usher in an era when anesthesia in hemodynamically impaired patients can be performed with relative safety predicated on proper selection of pharmacology for that purpose without concern for adverse clinical effects related to adrenal suppression or IMM.

Statement of the Use of Generative AI and AI-Assisted Technologies in the Writing Process

During the preparation of this manuscript, the author used ChatGPT in order to generate tables and images. After using this tool/service, the author reviewed and edited the content as needed and takes full responsibility for the content of the published article.

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References

1. Swerdlow B. Patient Safety Matters with Use of Propofol in Critically Ill Patients. *Cardiovasc. Sci.* **2025**, *2*, 10013. DOI:10.70322/cvs.2025.10013

2. Chen Y, Wu L, Lang B, Zhang W, Chen S. Recent progress in the development of etomidate analogues. *Front. Pharmacol.* **2025**, *16*, 1614865. DOI:10.3389/fphar.2025.1614865
3. Urman R, Malapero R, Zaccagnino M, Brovman E, Kaye A. Etomidate derivatives: Novel pharmaceutical agents in anesthesia. *J. Anaesthesiol. Clin. Pharmacol.* **2017**, *33*, 429. DOI:10.4103/0970-9185.222521
4. Kotani Y, Russotto V. Induction Agents for Tracheal Intubation in Critically Ill Patients. *Crit. Care Med.* **2025**, *53*, e173–e181. DOI:10.1097/CCM.0000000000006506
5. Ladha S, Prakash A. CON: Propofol Is Better Than Etomidate for Induction in Cardiac Surgical Patients. *J. Card. Crit. Care TSS* **2021**, *5*, 72–74. DOI:10.1055/s-0041-1728957
6. Valk BI, Struys MMRF. Etomidate and its Analogs: A Review of Pharmacokinetics and Pharmacodynamics. *Clin. Pharmacokinet.* **2021**, *60*, 1253–1269. DOI:10.1007/s40262-021-01038-6
7. Cagliani JA, Ruhemann A, Molmenti E, Smith C, Coppa G, Barrera R. Association between Etomidate Use for Rapid Sequence Intubation and Adrenal Insufficiency in Sepsis. *Cureus* **2021**, *13*, e13445. DOI:10.7759/cureus.13445
8. Upadhye S, Cyganik O. Is Single-Dose Etomidate Induction Safe in Emergency Intubation of Critically Ill Patients? *Ann. Emerg. Med.* **2016**, *67*, 399–400. DOI:10.1016/j.annemergmed.2015.10.006
9. Sarda BG, Raipure AM, Ruparel DH. Serum Cortisol Levels with Etomidate Induction. *Anesth. Essays Res.* **2021**, *15*, 312–315. DOI:10.4103/aer.aer_118_21
10. Komatsu R, You J, Rajan S, Kasuya Y, Sessler DI, Turan A. Steroid administration after anaesthetic induction with etomidate does not reduce in-hospital mortality or cardiovascular morbidity after non-cardiac surgery. *Br. J. Anaesth.* **2018**, *120*, 501–508. DOI:10.1016/j.bja.2017.11.079
11. Gu WJ, Wang F, Tang L, Liu JC. Single-Dose Etomidate Does Not Increase Mortality in Patients with Sepsis. *Chest* **2015**, *147*, 335–346. DOI:10.1378/chest.14-1012
12. Dalia AA, Raines DE. Etomidate and Adrenocortical Suppression: Should We Take the Concerns to Heart? *J. Cardiothorac. Vasc. Anesth.* **2021**, *35*, 1086–1088. DOI:10.1053/j.jvca.2021.01.034
13. Chittoria K, Sharma A. The novel etomidate analog: A potential induction agent. *Saudi J. Anaesth.* **2025**, *19*, 614–616. DOI:10.4103/sja.sja_503_25
14. Jung JH, Hyun B, Lee J, Koh DH, Kim JH, Park SW. Neurologic Safety of Etomidate-Based Sedation during Upper Endoscopy in Patients with Liver Cirrhosis Compared with Propofol: A Double-Blind, Randomized Controlled Trial. *J. Clin. Med.* **2020**, *9*, 2424. DOI:10.3390/jcm9082424
15. Luan HF, Zhao ZB, Feng JY, Cui JZ, Zhang XB, Zhu P, et al. Prevention of etomidate-induced myoclonus during anesthetic induction by pretreatment with dexmedetomidine. *Braz. J. Med. Biol. Res.* **2015**, *48*, 186–190. DOI:10.1590/1414-431x20144100
16. Geng D, Li Y, Wang C, Ren B, Wang H, Wu C, et al. Optimization, and *in vitro* and *in vivo* evaluation of etomidate intravenous lipid emulsion. *Drug Deliv.* **2021**, *28*, 873–883. DOI:10.1080/10717544.2021.1917729
17. Zhang KD, Wang LY, Zhang DX, Zhang ZH, Wang HL. Comparison of the Effectiveness of Various Drug Interventions to Prevent Etomidate-Induced Myoclonus: A Bayesian Network Meta-Analysis. *Front. Med.* **2022**, *9*, 799156. DOI:10.3389/fmed.2022.799156
18. McGrath M, Raines DE. Anesthetic Drug Discovery and Development: A Case Study of Novel Etomidate Analogs. *Methods Enzymol.* **2018**, *603*, 153–169. DOI:10.1016/bs.mie.2018.01.026
19. Forman SA, Warner DS. Clinical and Molecular Pharmacology of Etomidate. *Anesthesiology* **2011**, *114*, 695–707. DOI:10.1097/ALN.0b013e3181ff72b5
20. Zhao Y, Ai W, Zhao J, Yang X, Liu W, Ma Y, et al. From target specificity to metabolic efficiency: Design and optimization of etomidate analogues for potential improvement in postoperative outcomes. *Acta Pharm. Sin. B* **2026**, *16*, 2420–2443. DOI:10.1016/j.apsb.2026.01.008
21. Pejo E, Zhou X, Husain SS, Raines DE. Sedative-hypnotic Binding to 11β-hydroxylase. *Anesthesiology* **2016**, *125*, 943–951. DOI:10.1097/ALN.0000000000001304
22. Deng C, Liu J, Zhang W. Structural Modification in Anesthetic Drug Development for Prodrugs and Soft Drugs. *Front. Pharmacol.* **2022**, *13*, 923353. DOI:10.3389/fphar.2022.923353
23. Sneyd JR, Valk BI. Etomidate and its derivatives: Time to say goodbye? *Br. J. Anaesth.* **2025**, *134*, 11–13. DOI:10.1016/j.bja.2024.09.011
24. Yang J, Kang Y, Wang B, Yang L, Liu J, Zhang W. Metabolite-inactive etomidate analogues alleviating suppression on adrenal function in Beagle dogs. *Eur. J. Pharm. Sci.* **2017**, *99*, 343–349. DOI:10.1016/j.ejps.2016.12.041
25. Yang F, Ye P, Lv W, Li L, Zhao B, van denAnker J, et al. Methoxyethyl Etomidate Hydrochloride (ET-26): A Phase I Clinical Trial Assessing Drug–Drug Interactions in Healthy Subjects. *J. Clin. Pharmacol.* **2025**, *65*, 1443–1450. DOI:10.1002/jcph.70071

26. Jiang X, Yin Q, Deng X, Zhang W, Zhang W, Liu J. Advance of a new etomidate analogue—Methoxyethyl etomidate hydrochloride (ET-26) for anesthesia induction in surgical patients. *Anesthesiol. Periop. Sci.* **2024**, *2*, *22*. DOI:10.1007/s44254-024-00062-6
27. Liu X, Song H, Yang J, Zhou C, Kang Y, Yang L, et al. The etomidate analog ET-26 HCl retains superior myocardial performance: Comparisons with etomidate *in vivo* and *in vitro*. *PLoS ONE* **2018**, *13*, e0190994. DOI:10.1371/journal.pone.0190994
28. TrialX. A Trial to Evaluate the Efficacy and Safety of Methoxyetomidate Hydrochloride for Injection (ET-26) for the Induction of General Anesthesia in Elective Surgery Subjects. Available online: https://www.trialx.com/clinical-trials/listings/240953/a-trial-to-evaluate-7/ (accessed on 12 June 2026).
29. Miller TE, Gan TJ. Total Intravenous Anesthesia and Anesthetic Outcomes. *J. Cardiothorac. Vasc. Anesth.* **2015**, *29*, S11–S15. DOI:10.1053/j.jvca.2015.01.022
30. Yin Q, Yang Y, Liu J, Li L, Yang X, Diao L, et al. Phase 1 single-centre placebo- and etomidate-controlled study in healthy volunteers to assess safety, tolerability, clinical effects, and pharmacokinetics of intravenous methoxyethyl etomidate hydrochloride (ET-26). *Br. J. Anaesth.* **2025**, *134*, 80–88. DOI:10.1016/j.bja.2024.09.009
31. Orkaby A, Desai SP. The Death of Sodium Pentothal: The Rise and Fall of an Anesthetic Turned Lethal. *J. Hist. Med. Allied Sci.* **2021**, *76*, 294–318. DOI:10.1093/jhmas/jrab016
32. Xu X, Wei Y, Dong Y, Qiu Y, Mei Z, Wang K, et al. A Novel Etomidate Analog EL-0052 Retains Potent Hypnotic Effect and Stable Hemodynamics without Suppressing Adrenocortical Function. *J. Pharmacol. Exp. Ther.* **2021**, *379*, 324–330. DOI:10.1124/jpet.121.000691
33. Azad I, Khan T, Ahmad N, Khan AR, Akhter Y. Updates on Drug Designing Approach Through Computational Strategies: a Review. *Future Sci. OA* **2023**, *9*, FSO862. DOI:10.2144/fsoa-2022-0085